Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2	wo-9605863-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:37
L2	4	pct and "99" and "30393"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:38
L7	26028	hydrazide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L8	149	hydrazide and dox	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L9	4942	hydrazide and top	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L10	56	(hydrazide and dox) and (hydrazide and top)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L11	876	succinyl and prodrug	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L12	648	(succinyl and prodrug) and peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L13	785	succinyl same peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L14	11	(succinyl same peptide) same prodrug	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L15	2	WO-9605863-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L16	0	WO-9605863-$.did. and succinyl	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41

L17	2	"5962216".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L18	1	"5962216".pn. and succinyl	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L19	0	"09879442".did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
L20	0	"09879442".an.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
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L23	2	("6372712").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/06/23 14:41
L24	1	(("6372712").PN.) and hydrazide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/06/23 14:41
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L27	12	"00/33888"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2005/06/23 15:01
L28	6862	514/2.ccls.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2005/06/23 15:01
L29	3621	530/300,326330.ccls.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2005/06/23 15:03
L30	8811	530/300,326-330.ccls.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2005/06/23 15:03
L31	2	l30 and (therapeutic and $peptide and stabiliz$ and linker).clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	AND	ON	2005/06/23 15:04
S1	24278	hydrazide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 13:37
S2	123	hydrazide and dox	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/23 12:11
S3	4424	hydrazide and top	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/23 12:12
S4	48	(hydrazide and dox) and (hydrazide and top)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/23 12:12
S5	733	succinyl and prodrug	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 13:51
S6	552	(succinyl and prodrug) and peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 13:51

S7	694	succinyl same peptide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 13:52
S8	8	(succinyl same peptide) same prodrug	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 13:52
S9	2	WO-9605863-$.did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 13:52
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S11	2	"5962216".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 14:16
S12	1	"5962216".pn. and succinyl	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 15:01
S13	0	"09879442".did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 15:01
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S18	1	(("6372712").PN.) and hydrazide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/10/25 17:30

- Search History will be lost after eight hours of inactivity.
- To combine searches use # before search number, e.g., #2 AND #6.
- Search numbers may not be continuous; all searches are represented.
- Click on query # to add to strategy

Search	Most Recent Queries	Time	Result
#2	Search **succinyl prodrug**	17:01:25	22

Clear History

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FILE 'HOME' ENTERED AT 14:21:22 ON 23 JUN 2005

=> fil reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 14:21:32 ON 23 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES:   22 JUN 2005  HIGHEST RN 852803-45-3
DICTIONARY FILE UPDATES:  22 JUN 2005  HIGHEST RN 852803-45-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*************************************************************************
*                                                                       *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                       *
*************************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s
['bal''nal''aib'alm][lyfvwmpag'nle''nva''phg'][lfiagysft'nal''hse''bal'][alygstf'hs
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=> l2 and sql>=4

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nle''aib']/sqsp
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=> fil hcaplus; l4
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    66.78      66.99

FILE 'HCAPLUS' ENTERED AT 14:25:19 ON 23 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 23 Jun 2005  VOL 142 ISS 26
FILE LAST UPDATED: 22 Jun 2005  (20050622/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L5          879 L4

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         182509 THERAPEUTIC
          19129 THERAPEUTICS
         196869 THERAPEUTIC
                (THERAPEUTIC OR THERAPEUTICS)
L6           31 L5 AND THERAPEUTIC

=> l6 and conjugate
          60984 CONJUGATE
          53927 CONJUGATES
          94098 CONJUGATE
                (CONJUGATE OR CONJUGATES)
L7           11 L6 AND CONJUGATE

=> d l7 1-11 ibib abs hitstr

L7   ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:      2005:159927  HCAPLUS Full-text
DOCUMENT NUMBER:       142:254652
TITLE:                 Potentiation of the activation of high-molecular-
                       weight prodrugs for therapeutic or
                       diagnostic use
INVENTOR(S):           Trouet, Andre; Dubois, Vincent
PATENT ASSIGNEE(S):    Diatos, Fr.
```

SOURCE: Fr. Demande, 64 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2858936	A1	20050225	FR 2003-10114	20030822
WO 2005021043	A2	20050310	WO 2004-FR2162	20040819

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: FR 2003-10114 A 20030822

AB The invention discloses a modified form of a prodrug. The prodrugs of the invention include a bulky group, a spacer, a structure cleavable in the circulation, and a **therapeutic** agent or a marker. The spacer allows or facilitates the cleavage of the cleavable structure. Preparation of PEG-peptide-doxorubicin **conjugates** is included.

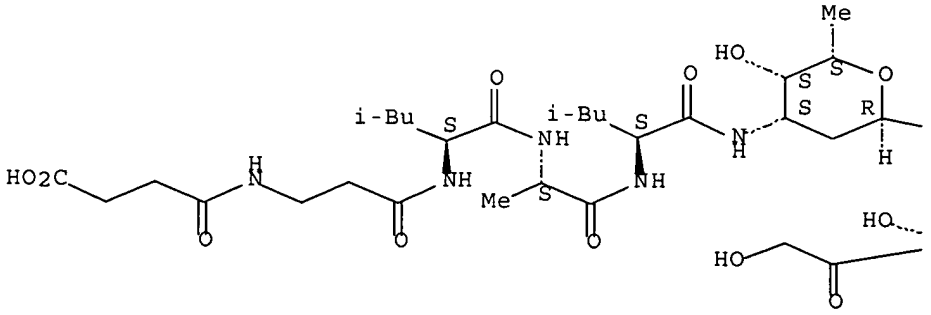
IT **274912-87-7**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(potentiation of activation of high-mol.-weight prodrugs for **therapeutic** or diagnostic use)

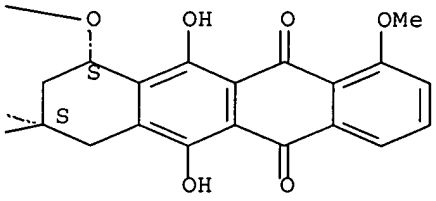
RN 274912-87-7 HCAPLUS

CN 5,12-Naphthacenedione, 10-[[3-[[N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



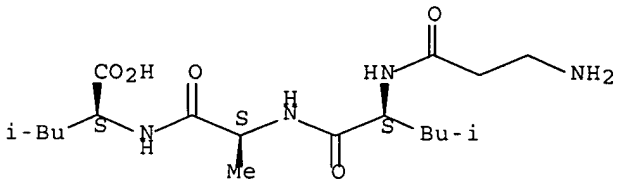


IT 177953-71-8DP, **conjugates** with PEG and doxorubicin
845815-56-7DP, **conjugates** with PEG and doxorubicin
845815-58-9DP, **conjugates** with PEG and doxorubicin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(potentiation of activation of high-mol.-weight prodrugs for **therapeutic** or diagnostic use)

RN 177953-71-8 HCAPLUS

CN L-Leucine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

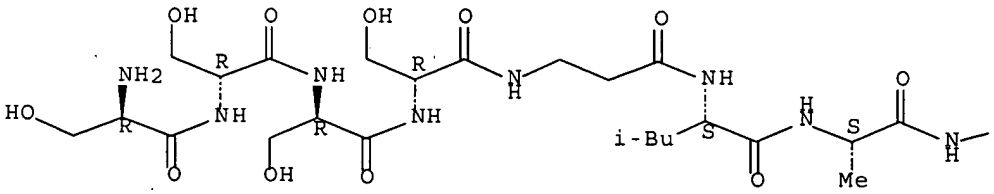
Absolute stereochemistry.

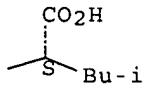


RN 845815-56-7 HCAPLUS

CN L-Leucine, D-seryl-D-seryl-D-seryl-D-seryl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

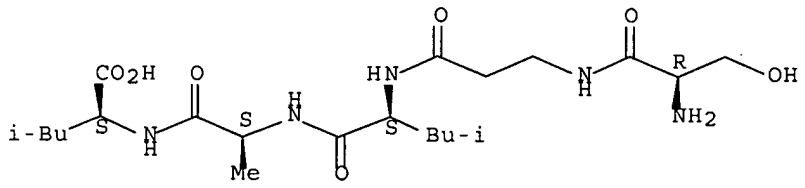
Absolute stereochemistry.





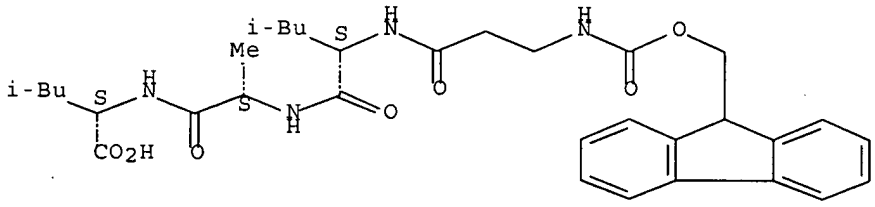
RN 845815-58-9 HCAPLUS
CN L-Leucine, D-seryl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **274912-97-9 845815-54-5 845815-55-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(potentiation of activation of high-mol.-weight prodrugs for **therapeutic** or diagnostic use)
RN 274912-97-9 HCAPLUS
CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 845815-54-5 HCAPLUS
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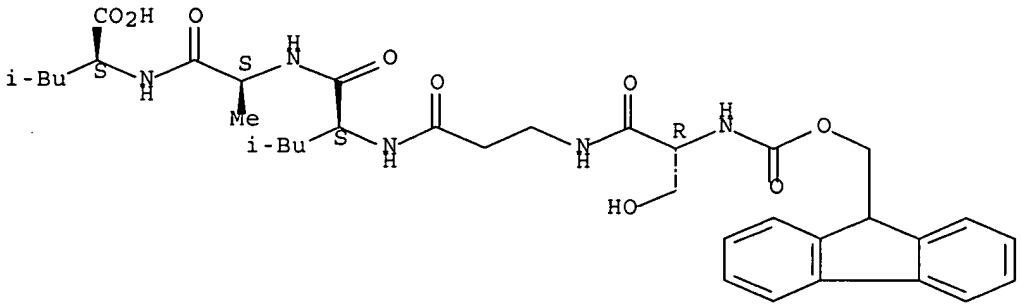
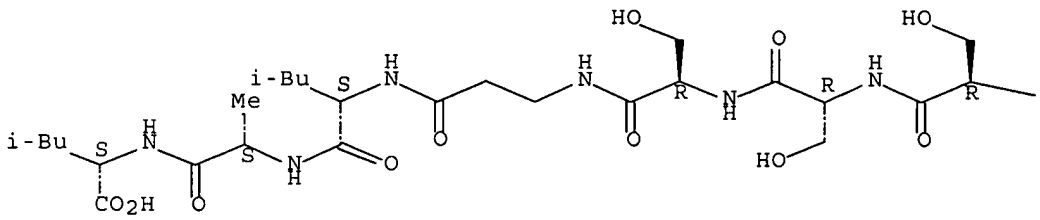
Absolute stereochemistry.



RN 845815-55-6 HCAPLUS
CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-D-seryl-D-seryl-D-seryl-D-seryl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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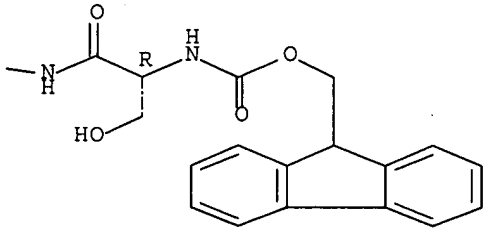


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:772189 HCAPLUS Full-text
DOCUMENT NUMBER: 140:8611
TITLE: Physical polymer matrixes based on affinity interactions between peptides and polysaccharides
AUTHOR(S): Seal, Brandon L.; Panitch, Alyssa
CORPORATE SOURCE: The Harrington Department of Bioengineering, Arizona State University, Tempe, AZ, 85287-9709, USA
SOURCE: Biomacromolecules (2003), 4(6), 1572-1582
CODEN: BOMAF6; ISSN: 1525-7797
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English

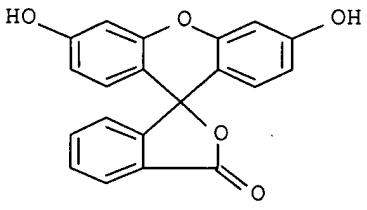
AB A rapidly forming polymer matrix with affinity-based controlled release properties was developed based upon interactions between heparin-binding peptides and heparin. Dynamic mech. testing of 10% (w/v) compns. consisting of a 3:1 molar ratio of poly(ethylene glycol)-co-peptide (.apprx.18 000 g/mol) to heparin (.apprx.18 000 g/mol) revealed a viscoelastic profile similar to that of concentrated, large mol. weight polymer solns. and melts. In addition, the biopolymer mixts. recovered quickly following thermal denaturation and mech. insult. These gel-like materials were able to sequester exogenous heparin-binding peptides and could release these peptides over several days at rates dependent on relative heparin affinity. The initial release rates ranged from 3.3% per h for a peptide with low heparin affinity to 0.025% per h for a peptide with strong heparin affinity. By altering the affinity of peptides to heparin, a series of peptides can be developed to yield a range of release profiles useful for controlled in vivo delivery of **therapeutics.**

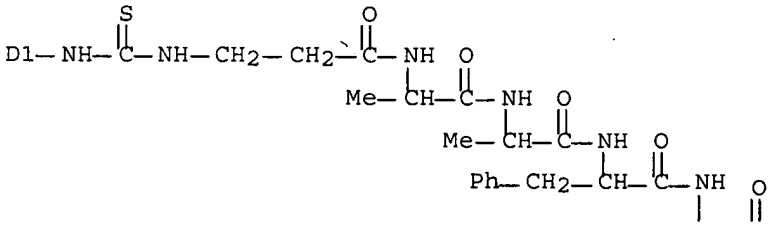
IT **627503-59-7DP**, reaction product with PEG vinyl sulfone
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phys. polymer matrixes based on affinity interactions between peptides and polysaccharides)

RN 627503-59-7 HCAPLUS

CN L-Alanine, N-[[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5(or 6)-yl]amino]thioxomethyl]-β-alanyl-L-alanyl-L-alanyl-L-phenylalanyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl-L-alanyl-L-arginyl-L-leucyl-L-tyrosyl-L-arginyl-L-lysyl- (9CI) (CA INDEX NAME)

PAGE 1-A





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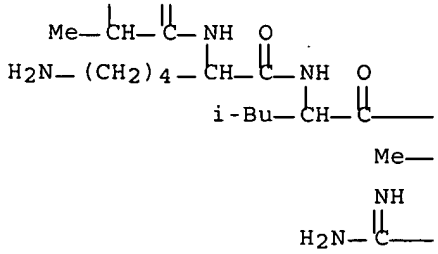

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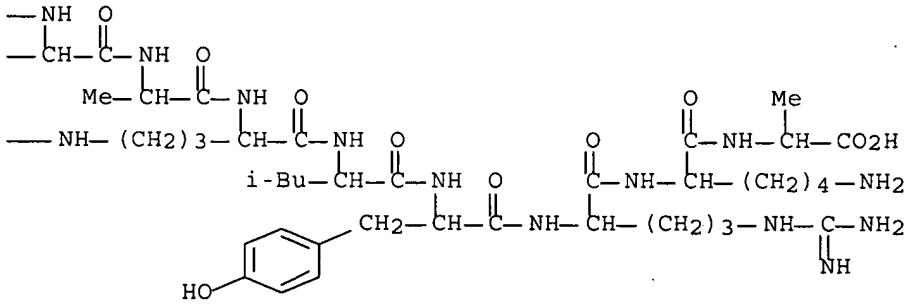
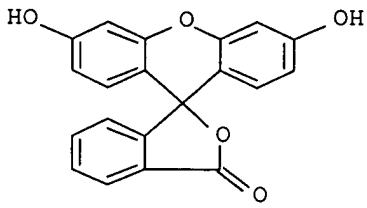
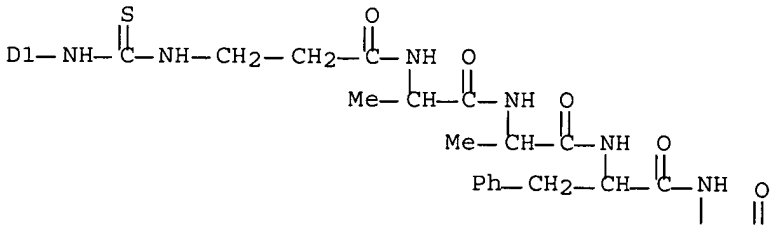


IT **627503-59-7P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(phys. polymer matrixes based on affinity interactions between peptides and polysaccharides)
RN 627503-59-7 HCAPLUS
CN L-Alanine, N-[[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5(or 6)-yl]amino]thioxomethyl]-β-alanyl-L-alanyl-L-alanyl-L-phenylalanyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl-L-alanyl-L-arginyl-L-leucyl-L-tyrosyl-L-arginyl-L-lysyl- (9CI) (CA INDEX NAME)

PAGE 1-A





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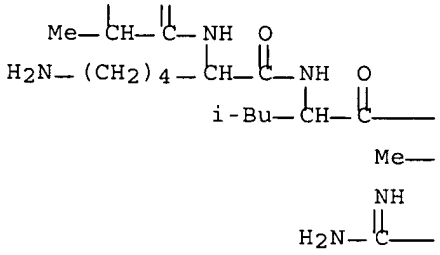

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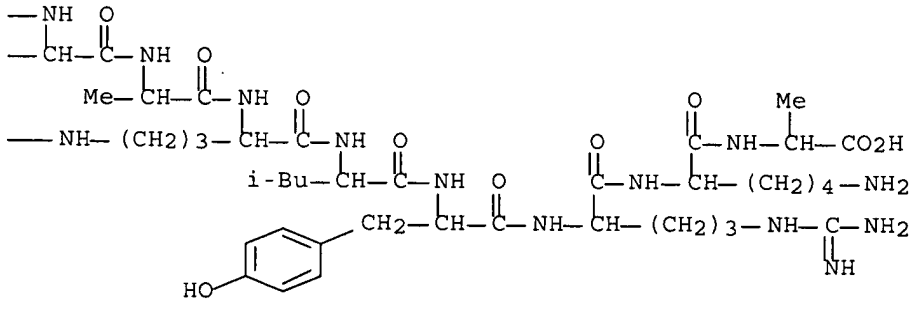

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:927432 HCAPLUS Full-text
DOCUMENT NUMBER: 138:4470
TITLE: Preparation of duocarmycin analogs as potent cytotoxins
INVENTOR(S): Ng, Howard P.; McGee, Danny P. C.; Wu, Guoxian; Li, Zhihong; Gangwar, Sanjeev; Saunders, Oliver L.; Martichonok, Valeri; Astafieva, Irina; Moore, Jimmie; Yarranton, Geoffrey Thomas; King, David J.; Boyd, Sharon; Lobl, Thomas J.
PATENT ASSIGNEE(S): Coulter Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096910	A1	20021205	WO 2002-US17210	20020531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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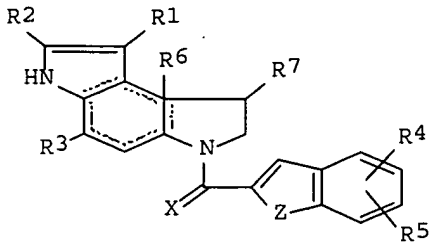
US 2003050331	A1	20030313	US 2002-160972	20020531
US 2003064984	A1	20030403	US 2002-161234	20020531
US 2003073852	A1	20030417	US 2002-161233	20020531
NZ 529788	A	20031219	NZ 2002-529788	20020531
EP 1434778	A1	20040707	EP 2002-731994	20020531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005500273	T2	20050106	JP 2003-500089	20020531
ZA 2003000735	A	20040623	ZA 2003-735	20030128

PRIORITY APPLN. INFO.:

US 2001-295196P	P	20010531
US 2001-295259P	P	20010531
US 2001-295342P	P	20010531
US 2001-304908P	P	20010711
WO 2002-US17210	W	20020531

OTHER SOURCE(S): MARPAT 138:4470
GI



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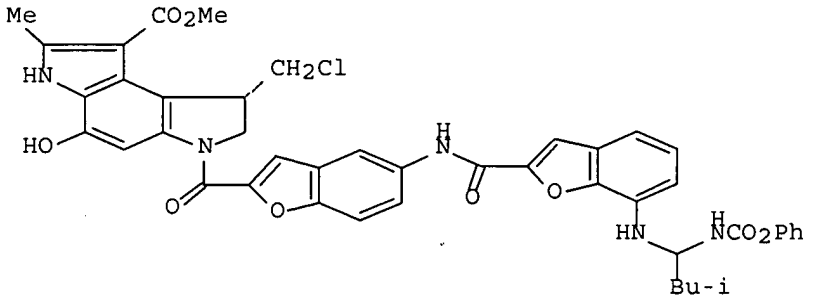


II

AB Duocarmycin analogs I [X, Z = O, S, or imino; R1 = H, (un)substituted alkyl, carboxylic acid, ester, or amide; R2 = H, (un)subsituted alkyl; R3 = :O, OH or derivative; R4, R5 = H, (un)substituted alkyl, (hetero)aryl, heterocycloalkyl, halo, NO2, NR15R16, NCOR15, O2CNR15R16, OCO2R15,COR5, OR15, where R15 and R16 = H, (un)substituted (hetero)alkyl, (hetero)aryl, heterocycloalkyl, or peptidyl or NR15R16 = (un)substituted 4-6 membered heterocycloalkyl; R6 = a single bond; R7 = CH2-X, where X is a leaving group; or R6 and R7 may form a cyclopropyl ring] were prepared as potent cytotoxins. Peptidyl and disulfide linkers are cleaved in vivo. The linkers are of use in forming prodrugs and **conjugates** of the cytotoxins of the invention as well as other diagnostic and **therapeutic** moieties. Thus, compound II was prepared via acylation of the 5-amino-2-benzoyl intermediate. Compds. I generally have an IC50 value in a proliferation assay of .apprx. 1-100 nM, preferably .apprx. 10-10 nM.

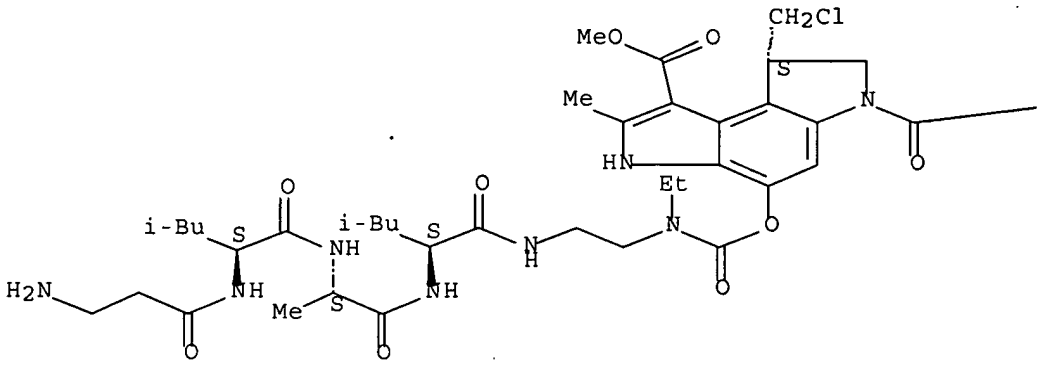
IT **477207-78-6P 477207-81-1P 477207-82-2P**
477207-83-3P 477207-84-4P 477207-86-6P
477209-21-5P 477209-22-6P 477209-52-2P
477209-54-4P 477209-56-6P 477209-59-9P
477209-60-2P 477209-61-3P 477209-62-4P
477209-63-5P 477209-64-6P 477209-66-8P
477209-67-9P 477209-68-0P 477209-69-1P
477328-57-7P 477328-58-8P 477328-60-2P
477328-61-3P 477328-62-4P 477328-63-5P
477328-64-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of duocarmycin analogs as potent cytotoxins)

RN 477207-78-6 HCAPLUS

CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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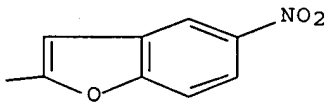
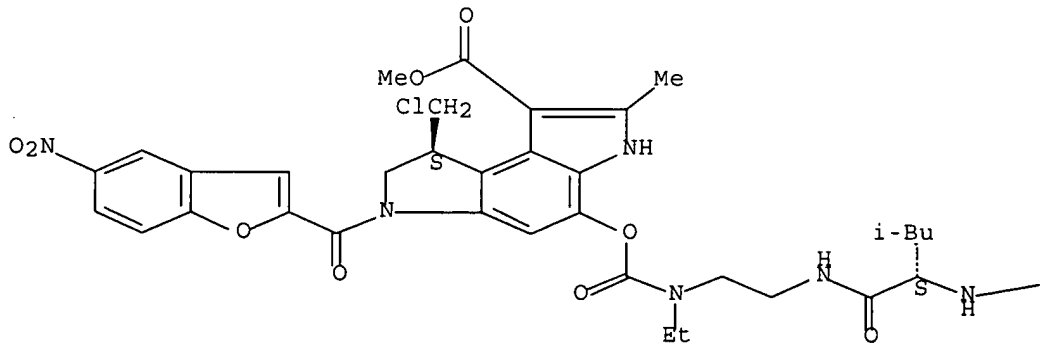


RN 477207-81-1 HCAPLUS

CN L-Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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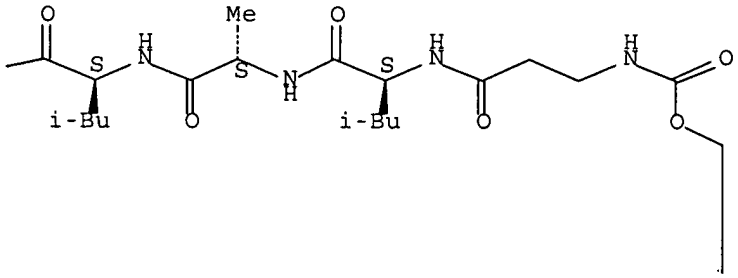

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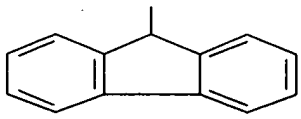
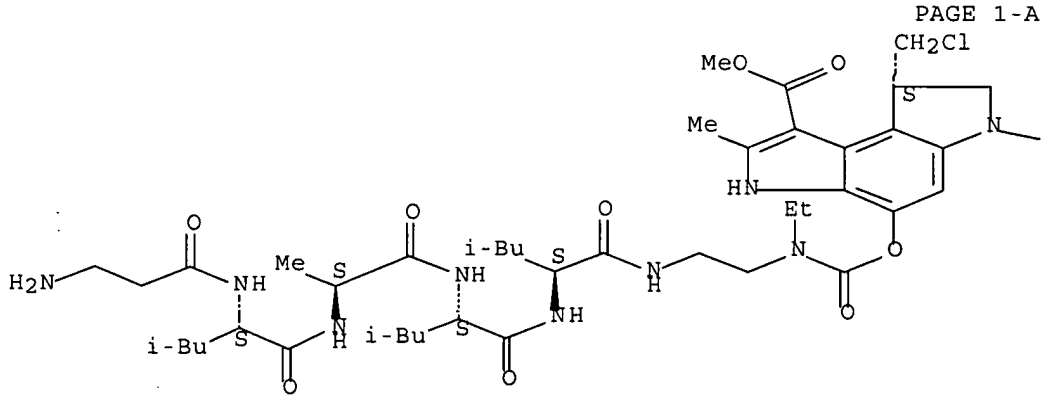


RN 477207-82-2 HCAPLUS

CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-L-leucyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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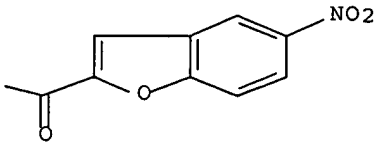
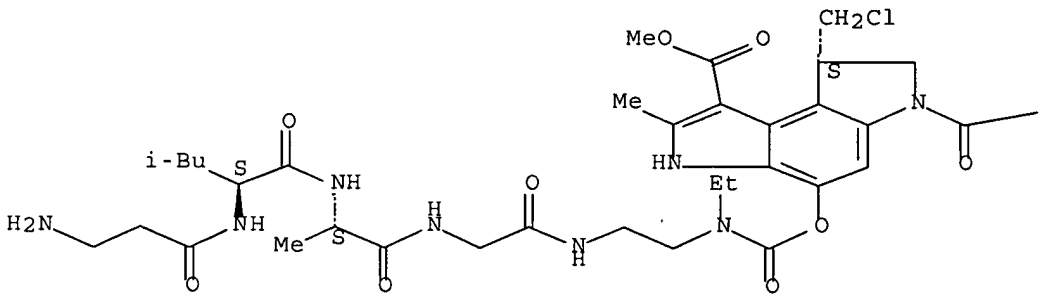


RN 477207-83-3 HCAPLUS

CN Glycinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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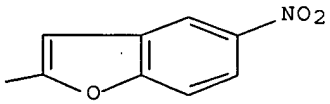
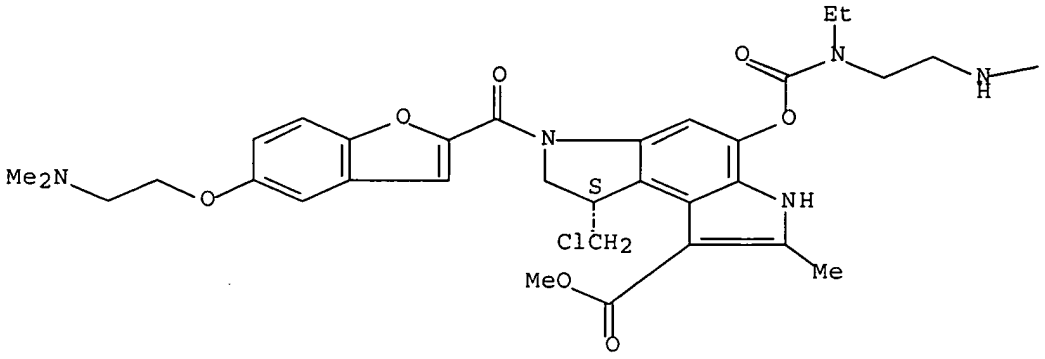


RN 477207-84-4 HCAPLUS

CN L-Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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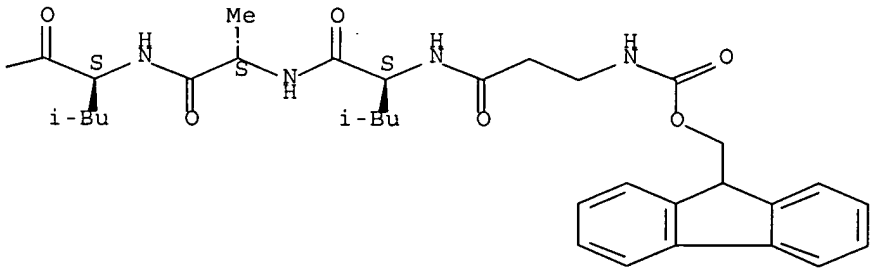
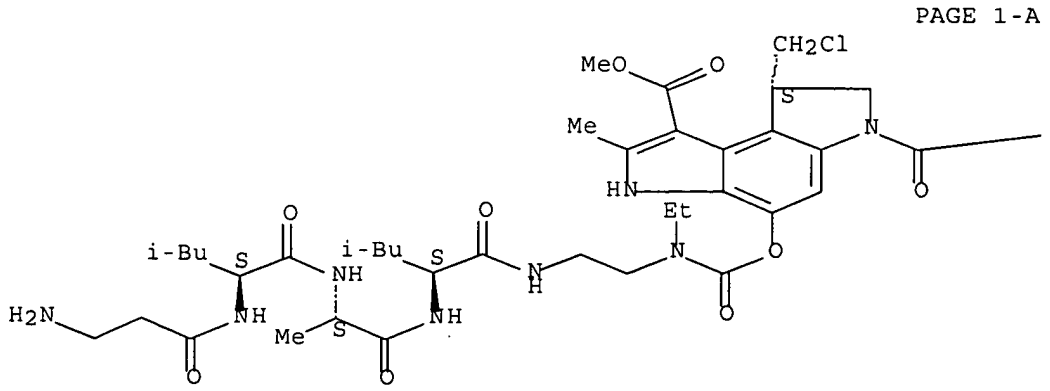


RN 477207-86-6 HCAPLUS

CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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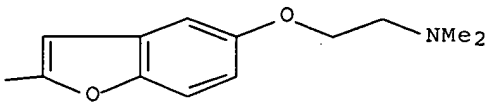
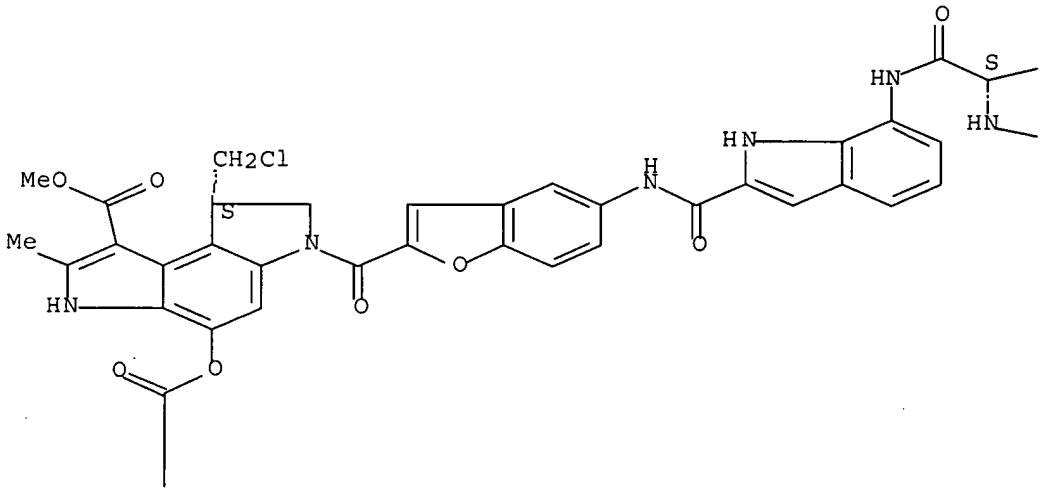


RN 477209-21-5 HCAPLUS

CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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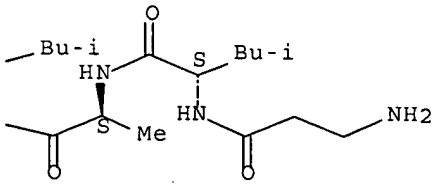
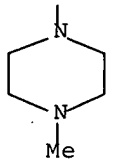
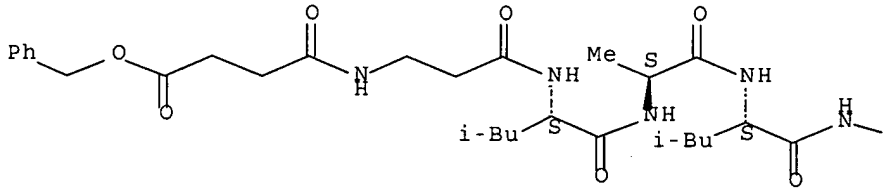


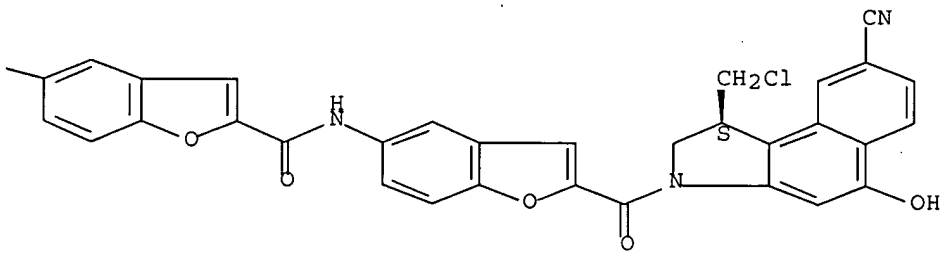


RN 477209-22-6 HCAPLUS

CN L-Leucinamide, N-[1,4-dioxo-4-(phenylmethoxy)butyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



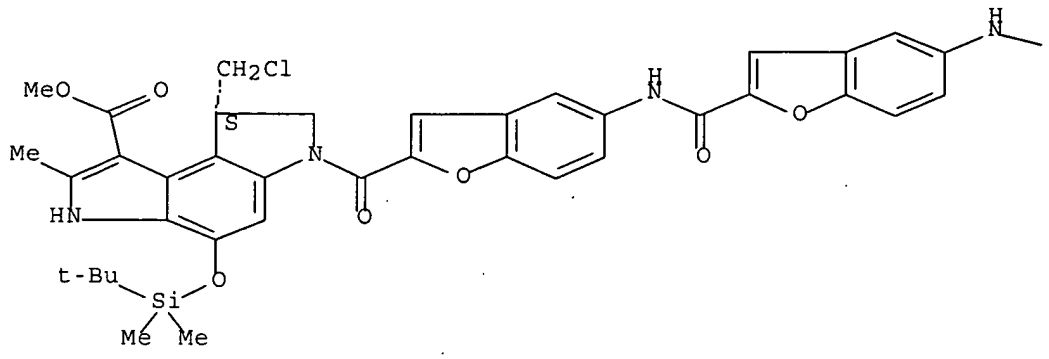


RN 477209-52-2 HCAPLUS

CN L-Leucinamide, N-[1,4-dioxo-4-(phenylmethoxy)butyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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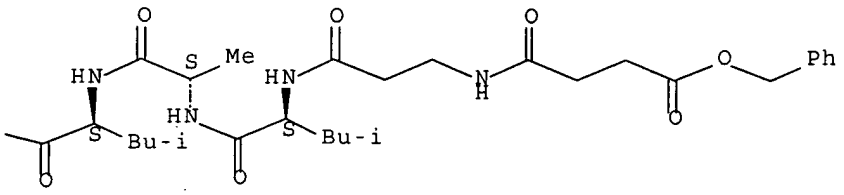
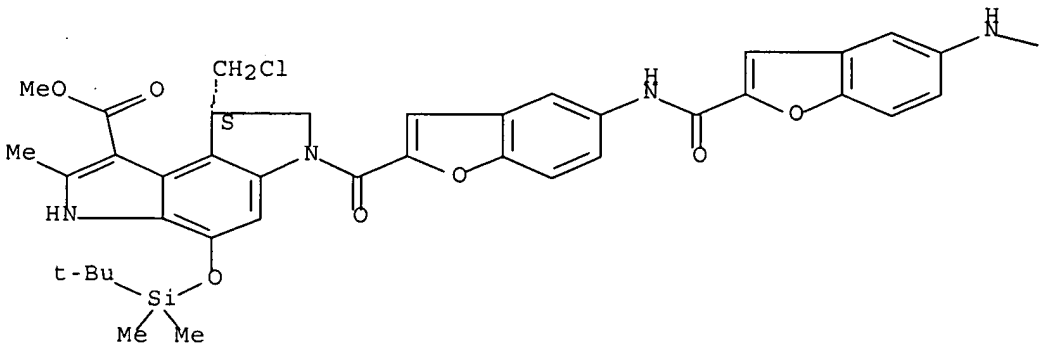


RN 477209-54-4 HCAPLUS

CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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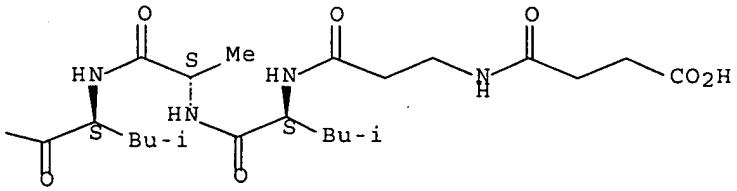
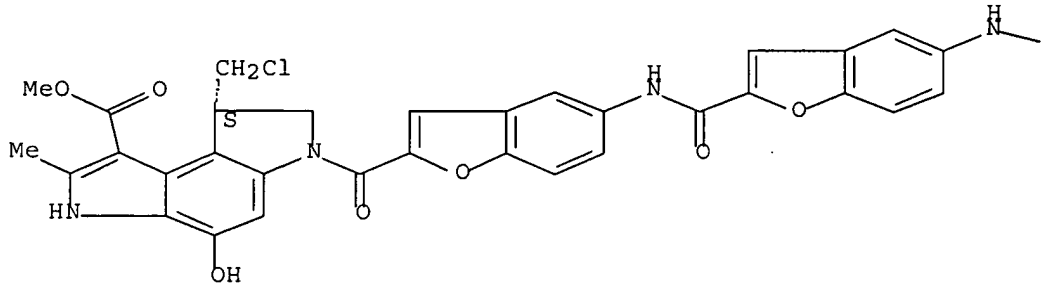


RN 477209-56-6 HCAPLUS

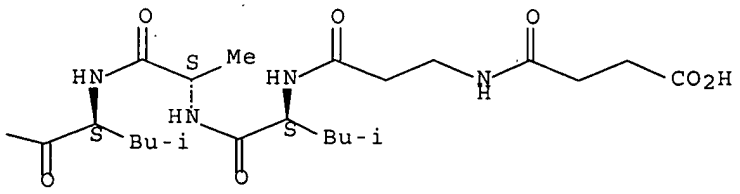
CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

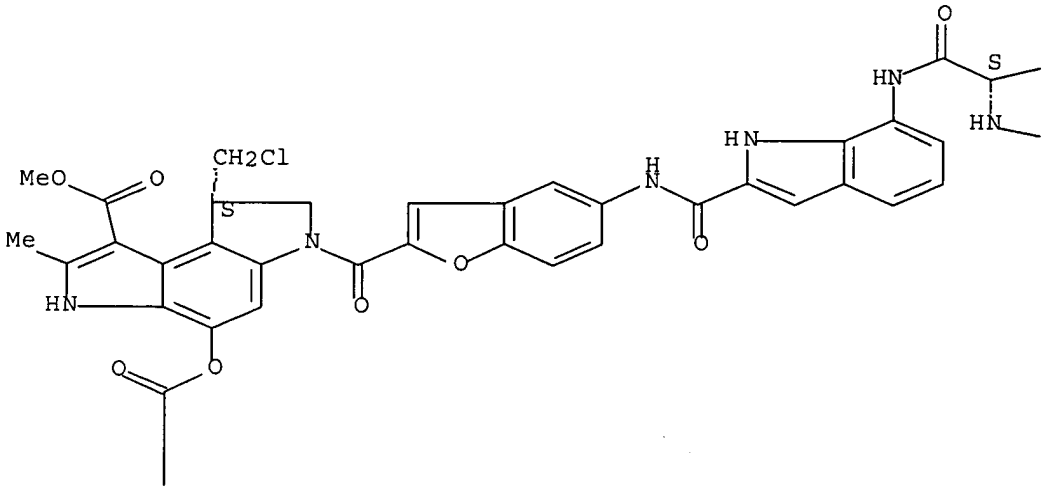


RN 477209-59-9 HCAPLUS

CN L-Leucinamide, N-(5-carboxy-1-oxopentyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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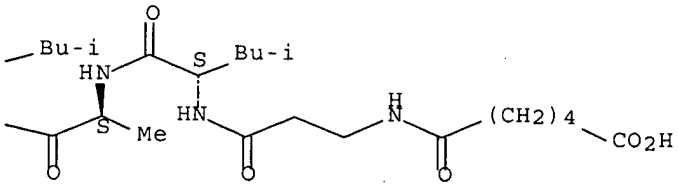
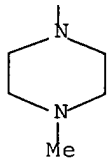


PAGE 2-A

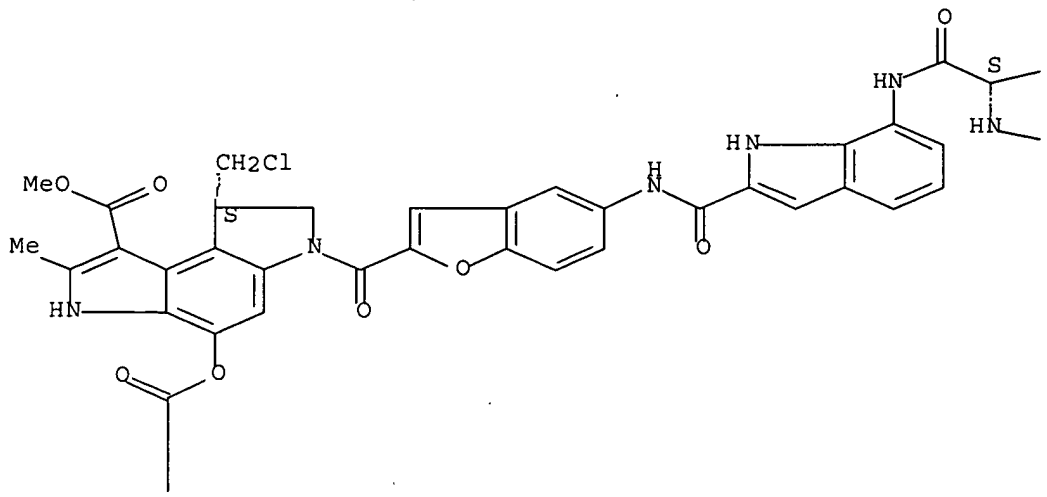


RN 477209-60-2 HCAPLUS

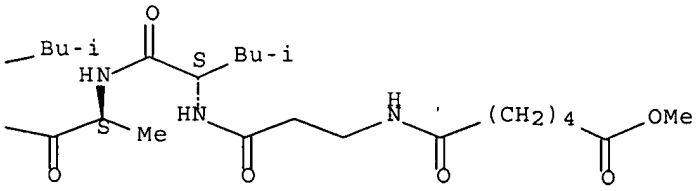
CN L-Leucinamide, N-(6-methoxy-1,6-dioxohexyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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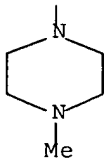

RN 477209-61-3 HCAPLUS

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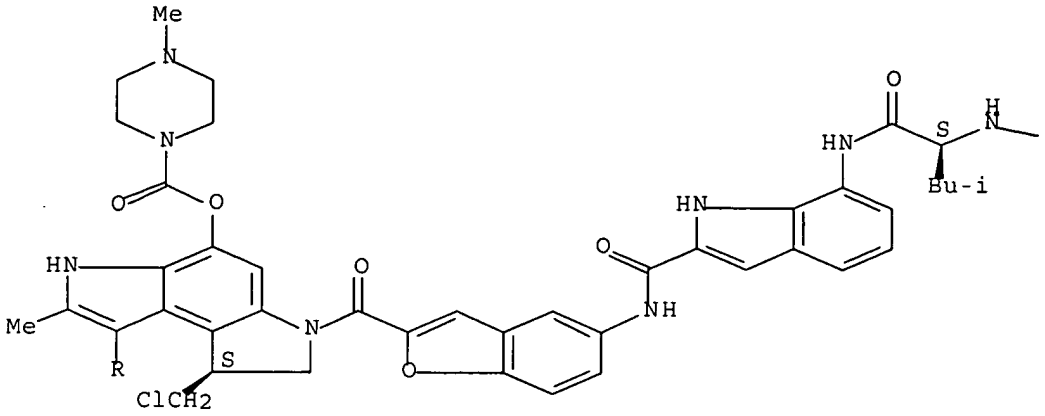
Absolute stereochemistry.

PAGE 1-A



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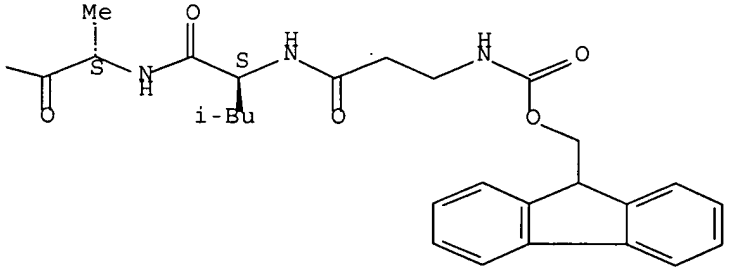

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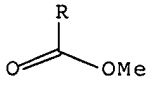
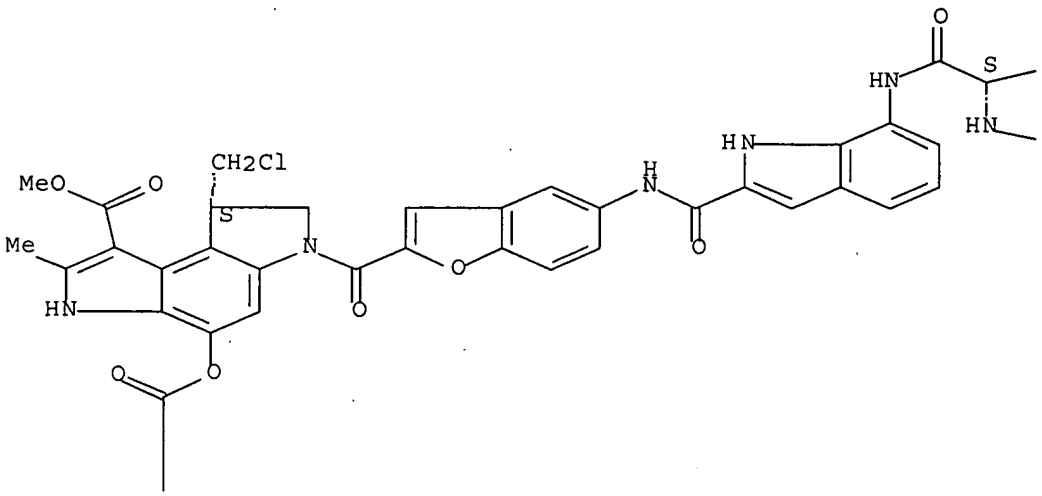


RN 477209-62-4 HCAPLUS

CN L-Leucinamide, N-[1,6-dioxo-6-(phenylmethoxy)hexyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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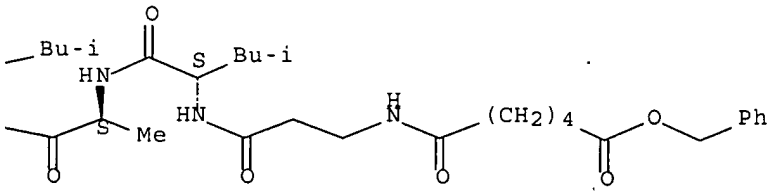
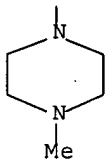


PAGE 2-A

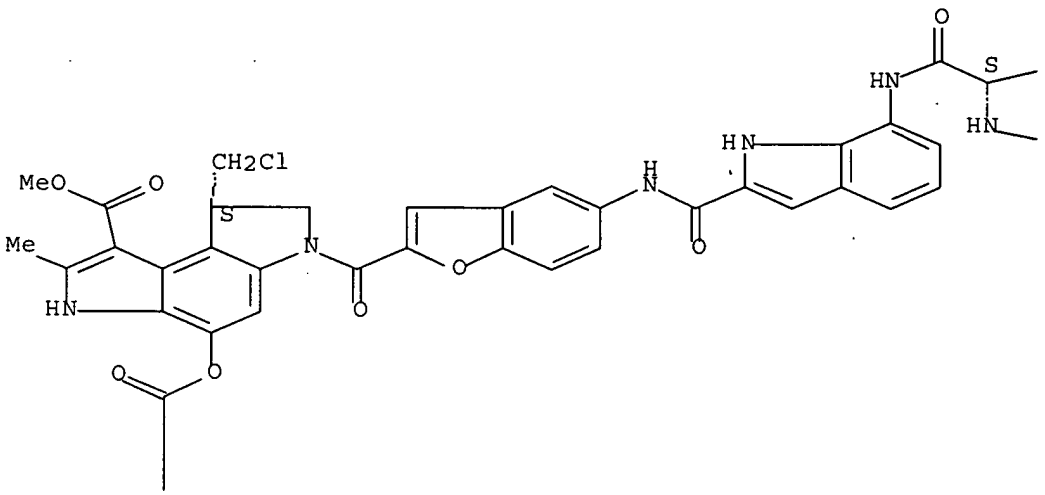


RN 477209-63-5 HCAPLUS

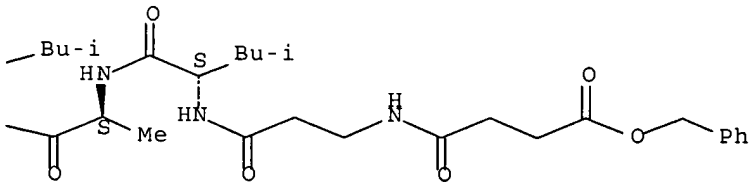
CN L-Leucinamide, N-[1,4-dioxo-4-(phenylmethoxy)butyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

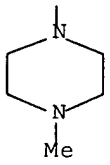
PAGE 1-A



PAGE 1-B



PAGE 2-A

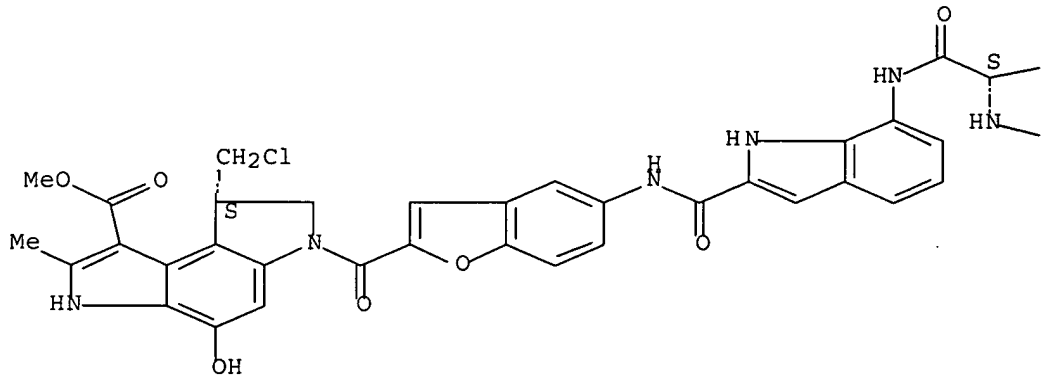


RN 477209-64-6 HCAPLUS

CN L-Leucinamide, N-(5-carboxy-1-oxopentyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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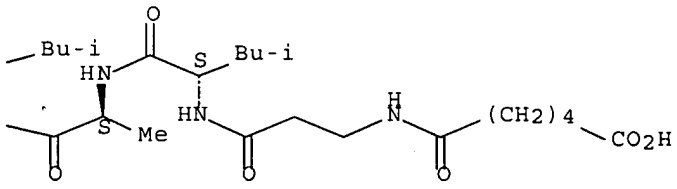
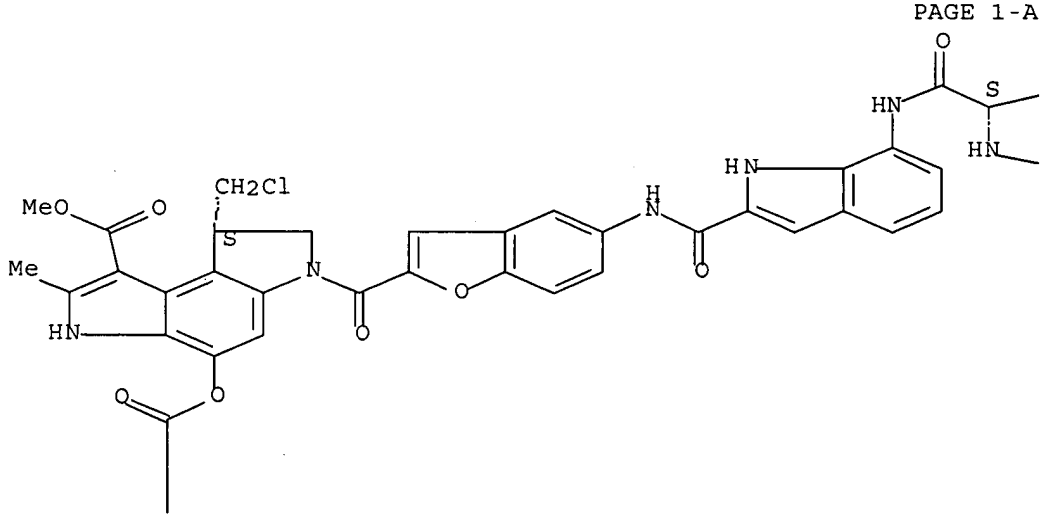


RN 477209-66-8 HCAPLUS

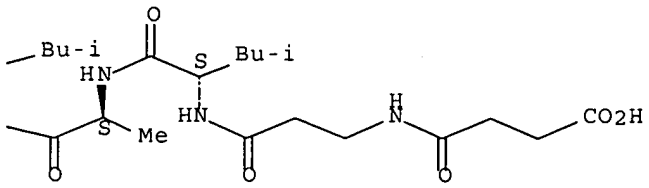
CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

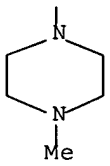
PAGE 1-A



PAGE 1-B



PAGE 2-A

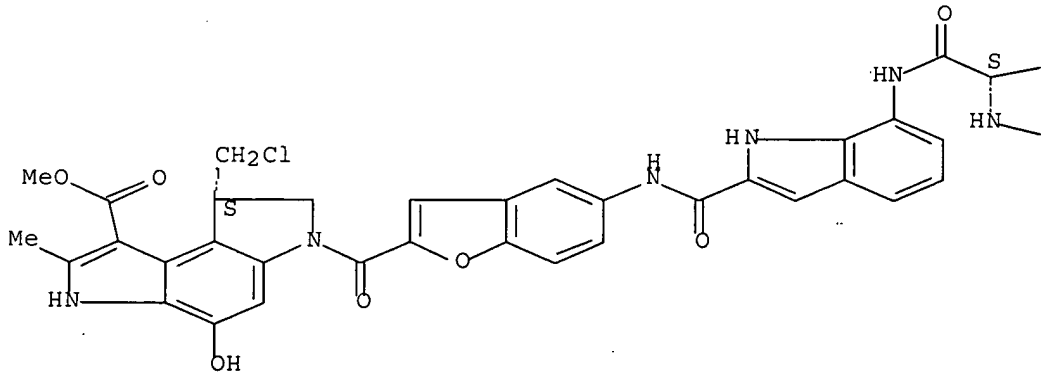


RN 477209-67-9 HCAPLUS

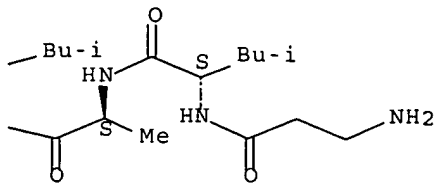
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

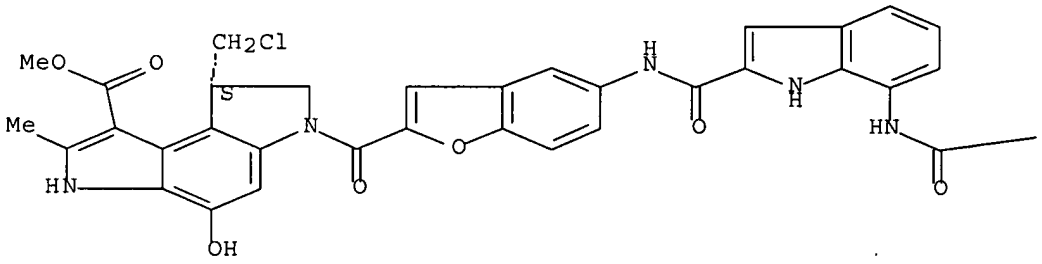


RN 477209-68-0 HCAPLUS

CN L-Leucinamide, N-[(1-methyl-4-piperidinyl)carbonyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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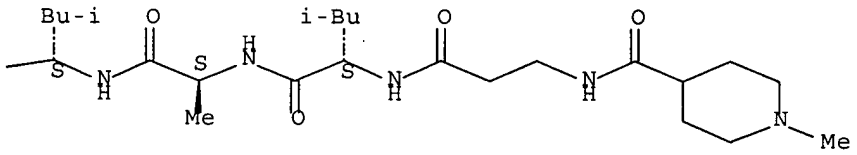
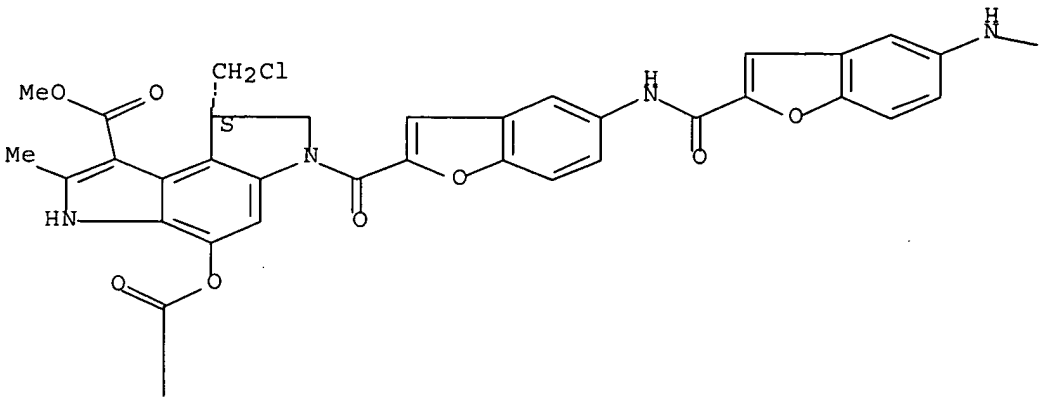


RN 477209-69-1 HCAPLUS

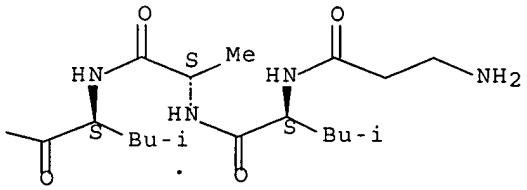
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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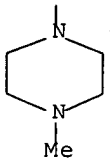
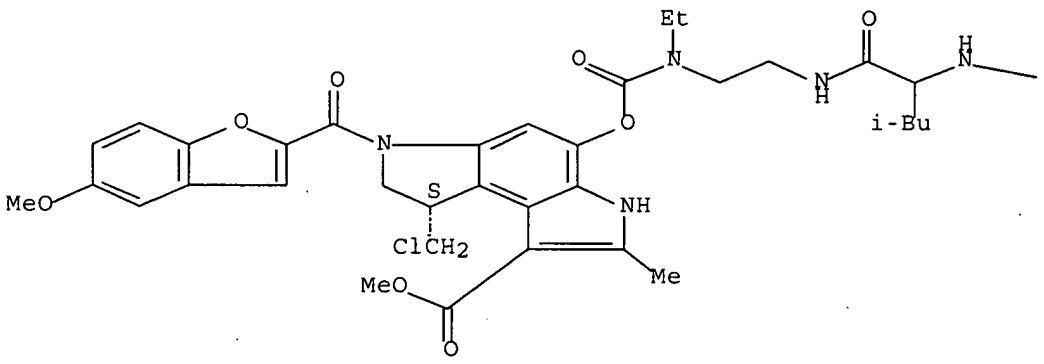


RN 477328-57-7 HCAPLUS

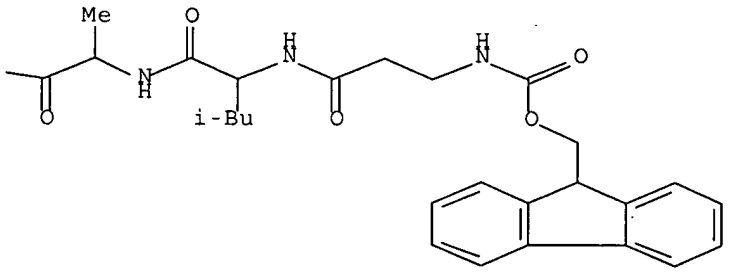
CN Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanylleucylalanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

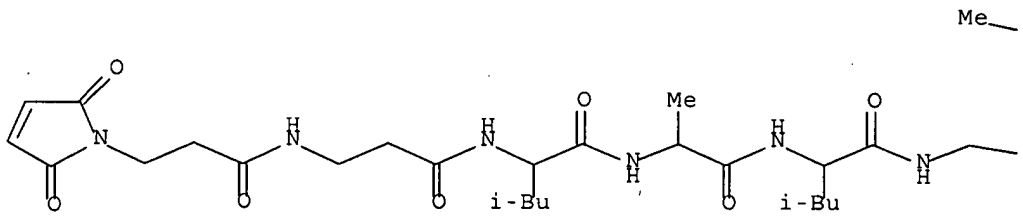


RN 477328-58-8 HCAPLUS

CN Leucinamide, N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-β-alanylleucylalanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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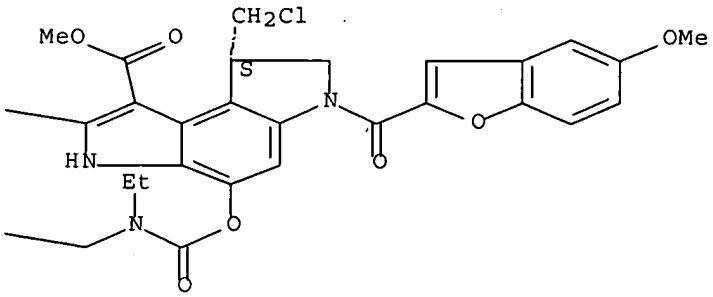
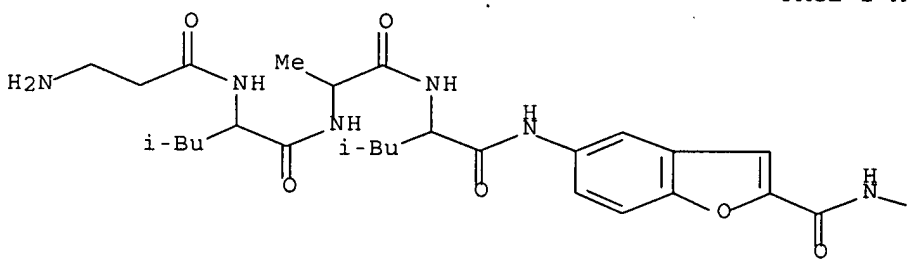


RN 477328-60-2 HCAPLUS

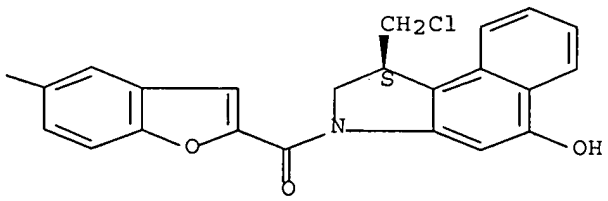
CN Leucinamide, β-alanylleucylalanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

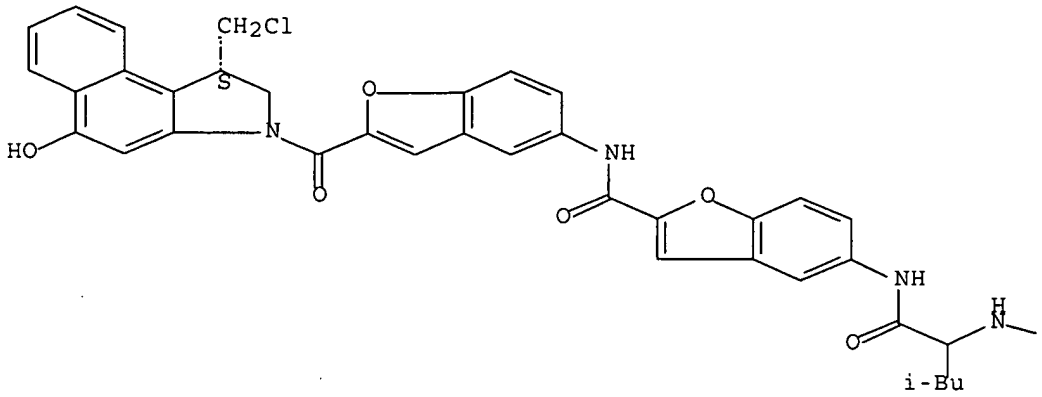


RN 477328-61-3 HCAPLUS

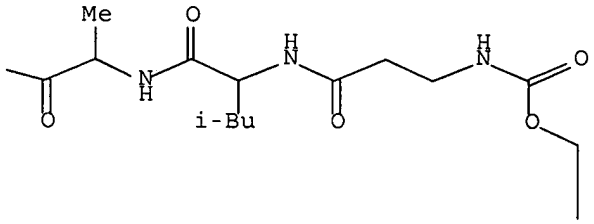
CN Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanylleucylalanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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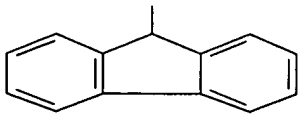
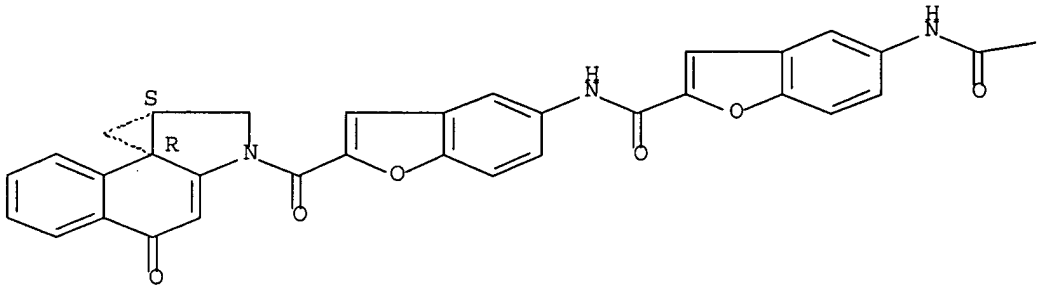


RN 477328-62-4 HCAPLUS

CN Leucinamide, β-alanylleucylalanyl-N-[2-[[[2-[[(8bR,9aS)-9,9a-dihydro-4-oxo-1H-benzo[e]cycloprop[c]indol-2(4H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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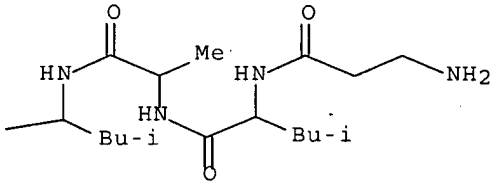
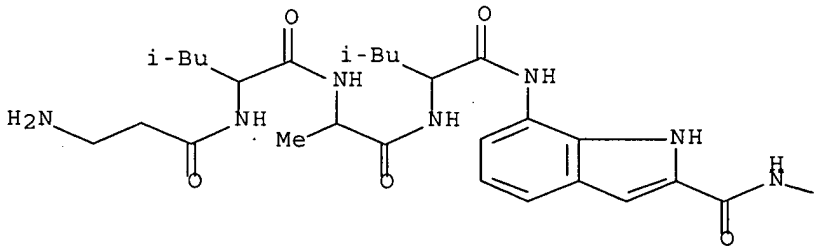


RN 477328-63-5 HCAPLUS

CN Leucinamide, β-alanylleucylalanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-8-cyano-1,2-dihydro-5-hydroxy-3H-benz[e]indol-3-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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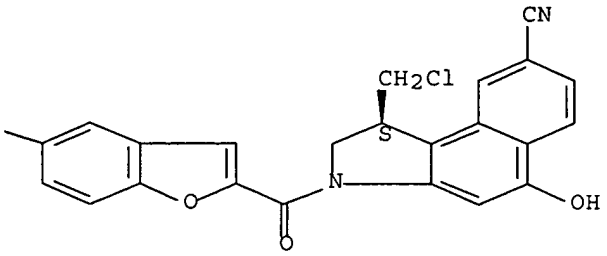
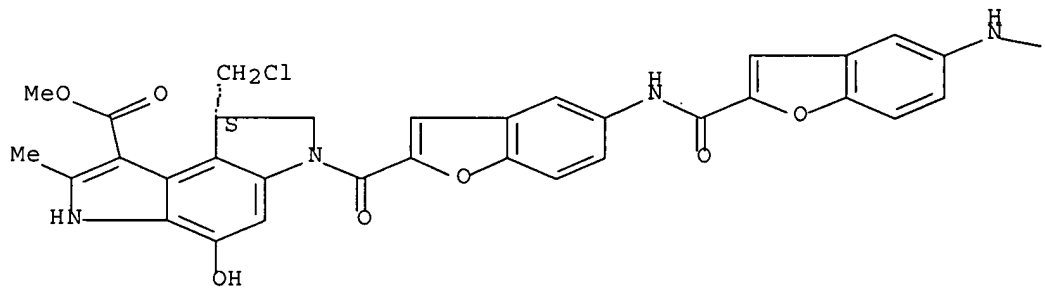


RN 477328-64-6 HCAPLUS

CN Leucinamide, N-(3-carboxy-1-oxopropyl)-β-alanylleucylalanyl-N-[6-[[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-5-hydroxy-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]amino]-6-oxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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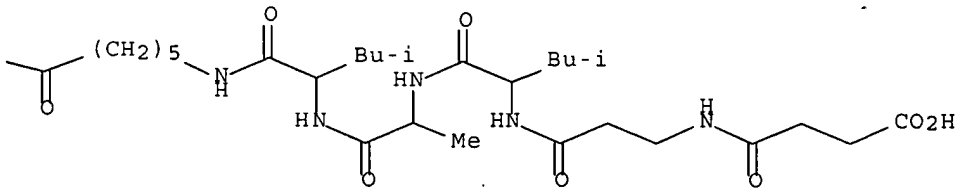


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:755199 HCAPLUS Full-text

DOCUMENT NUMBER: 137:284323

TITLE: Enzyme-cleavable prodrug compounds

INVENTOR(S): Dubois, Vincent; Fernandez, Anne Marie; Gangwar,

Sanjeev; Lewis, Evan; Lobl, Thomas J.; Nieder, Matthew H.; Pickford, Lesley B.; Trouet, Andre; Yarranton, Geoffrey T.

PATENT ASSIGNEE(S): Belg.

SOURCE: U.S. Pat. Appl. Publ., 86 pp., Cont.-in-part of Appl. No. PCT/US99/30393.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002142955	A1	20021003	US 2001-879442	20010611
WO 2000033888	A2	20000615	WO 1999-US30393	19991210
WO 2000033888	A3	20011108		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1998-111793P	P	19981211
US 1999-119312P	P	19990208
WO 1999-US30393	A2	19991210
US 2000-211887P	P	20000614
US 2001-290448P	P	20010511

OTHER SOURCE(S): MARPAT 137:284323

AB The prodrug of the invention is a modified form of a **therapeutic** agent and comprises a **therapeutic** agent, an oligopeptide, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by the enzyme Thimet oligopeptidase, or TOP. Also disclosed are methods of designing prodrugs by utilizing TOP-cleavable sequences within the **conjugate** and methods of treating patients with prodrugs of the invention.

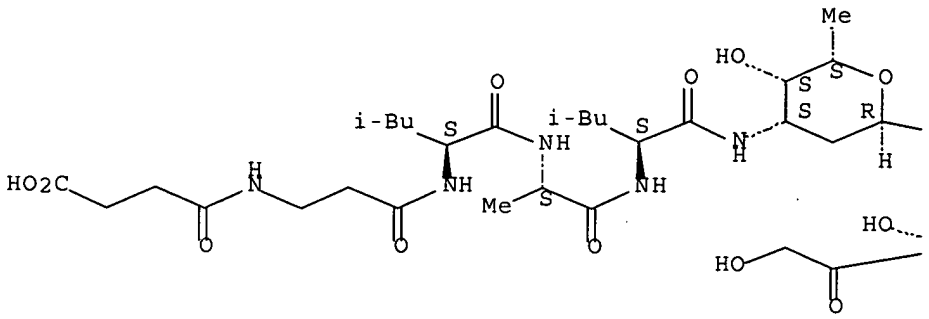
IT **274912-87-7P 274912-88-8P 274912-89-9P**
RL: BSU (Biological study, unclassified); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thimet oligopeptidase-cleavable prodrug compds.)

RN 274912-87-7 HCAPLUS

CN 5,12-Naphthacenedione, 10-[[3-[[N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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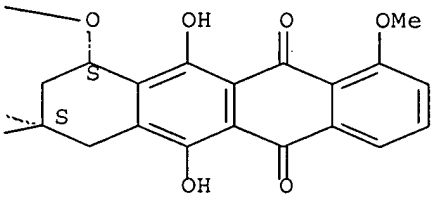
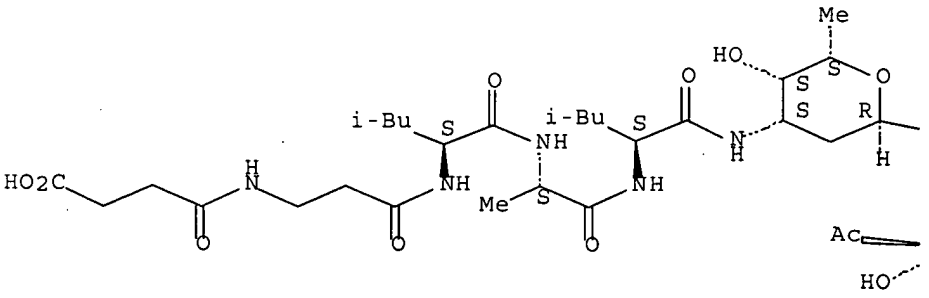


RN 274912-88-8 HCAPLUS

CN 5,12-Naphthacenedione, 8-acetyl-10-[[3-[[N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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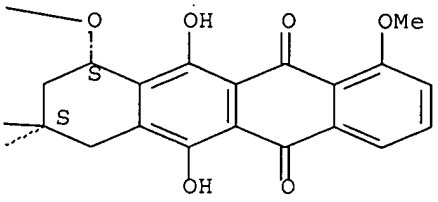
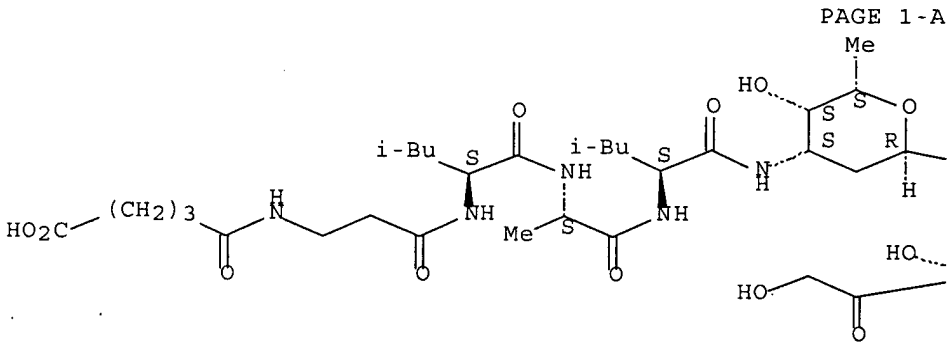


RN 274912-89-9 HCAPLUS

CN 5,12-Naphthacenedione, 10-[[3-[[N-(4-carboxy-1-oxobutyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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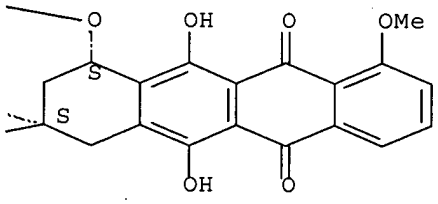


IT 177953-52-5P 274912-90-2P 274912-91-3P
274912-92-4P 274912-93-5P 274912-94-6P
274912-95-7P 274912-96-8P 274912-97-9P
274912-99-1P 274913-02-9P 274913-03-0P

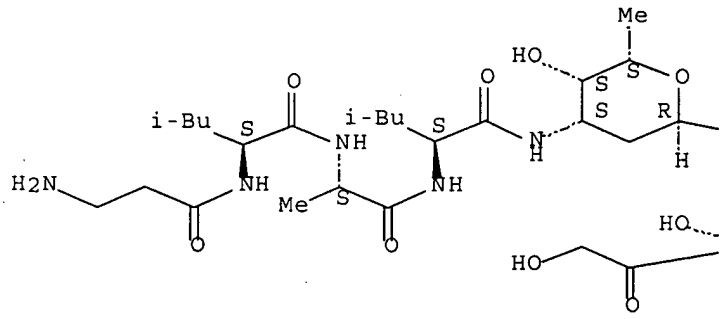
274913-04-1P 274913-05-2P 274913-06-3P
274913-07-4P
RL: BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thimet oligopeptidase-cleavable prodrug compds.)

RN 177953-52-5 HCAPLUS

CN 5,12-Naphthacenedione, 10-[[3-[(β-alanyl-L-leucyl-L-alanyl-L-leucyl)amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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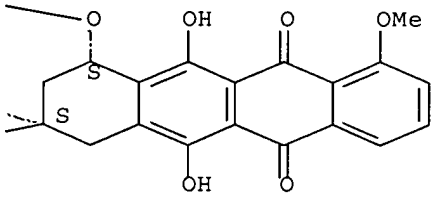
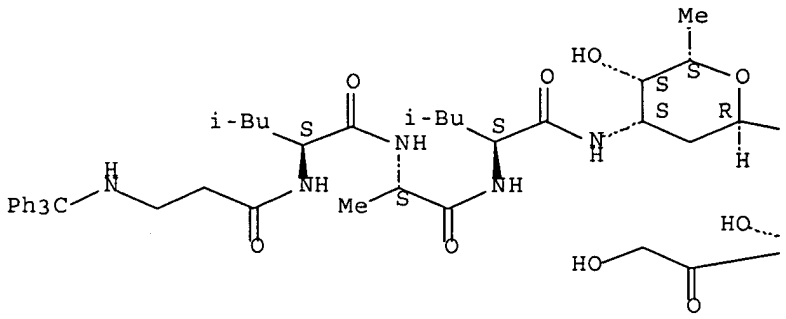


RN 274912-90-2 HCAPLUS

CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-(triphenylmethyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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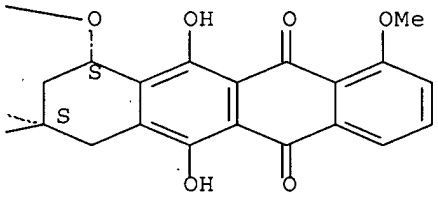
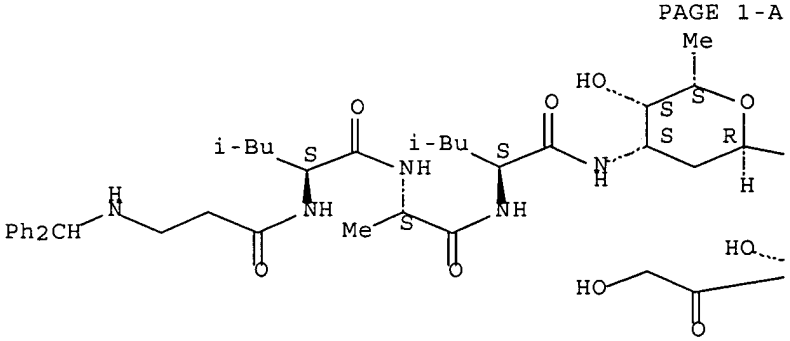


RN 274912-91-3 HCAPLUS

CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-(diphenylmethyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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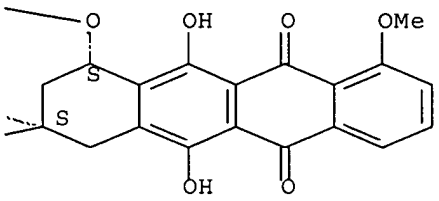

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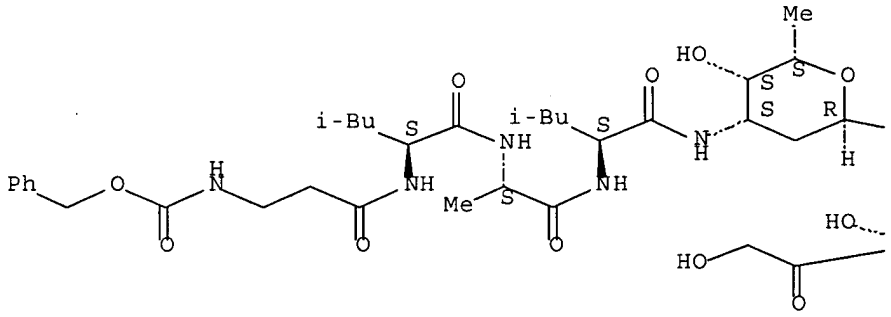
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-[(phenylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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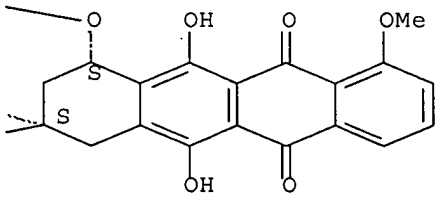
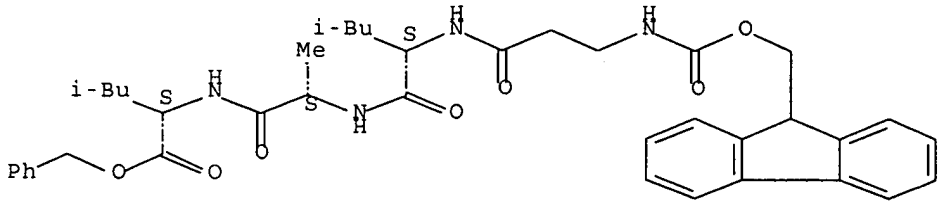


RN 274912-93-5 HCAPLUS
CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

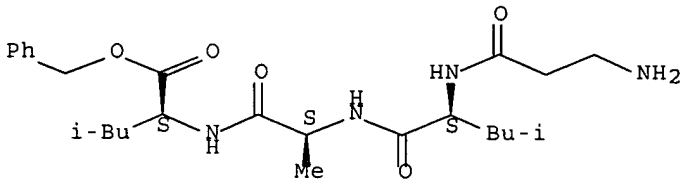
Absolute stereochemistry.



RN 274912-94-6 HCAPLUS

CN L-Leucine, β-alanyl-L-leucyl-L-alanyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

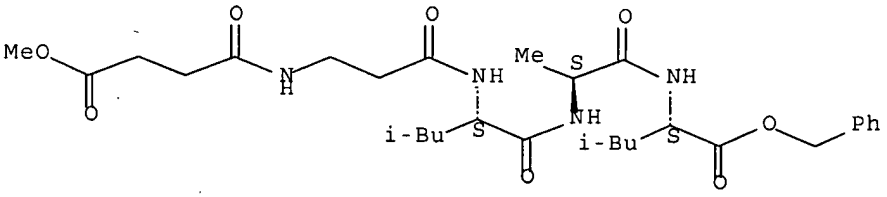
Absolute stereochemistry.



RN 274912-95-7 HCAPLUS

CN L-Leucine, N-(4-methoxy-1,4-dioxobutyl)-β-alanyl-L-leucyl-L-alanyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

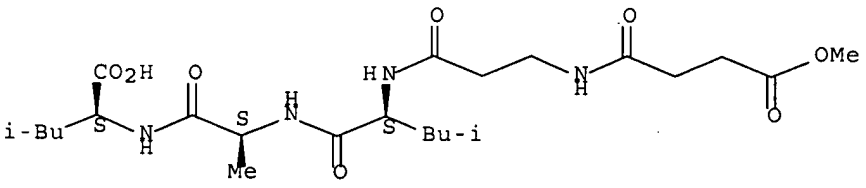
Absolute stereochemistry.



RN 274912-96-8 HCAPLUS

CN L-Leucine, N-(4-methoxy-1,4-dioxobutyl)-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

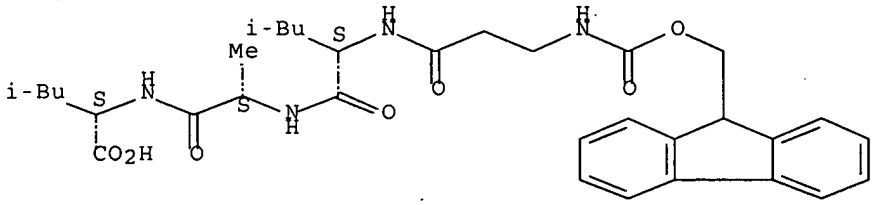
Absolute stereochemistry.



RN 274912-97-9 HCAPLUS

CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

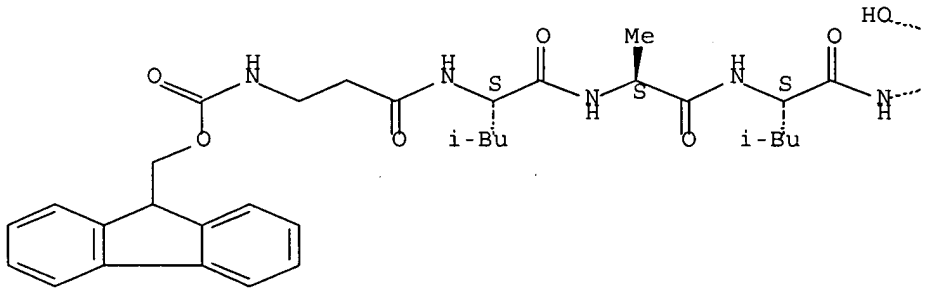


RN 274912-99-1 HCAPLUS

CN 5,12-Naphthacenedione, 8-acetyl-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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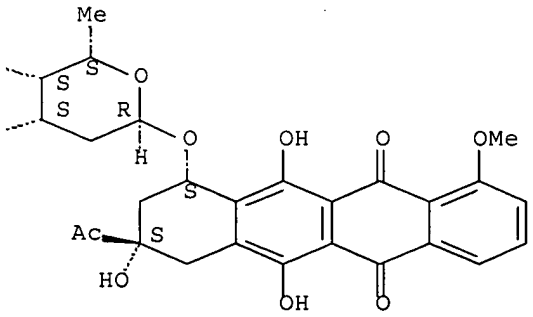


RN 274913-02-9 HCAPLUS

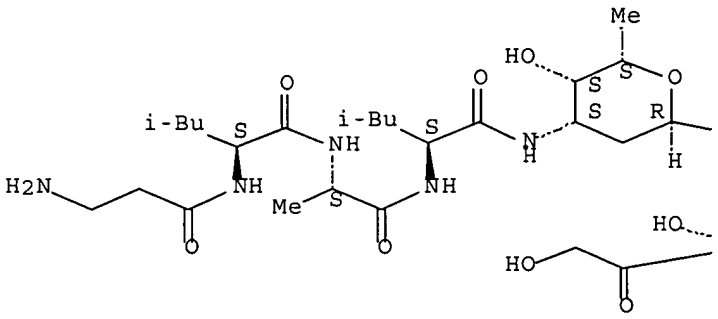
CN Propanoic acid, 2-hydroxy-, compd. with (8S,10S)-10-[[3-[(β-alanyl-L-leucyl-L-alanyl-L-leucyl)amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 177953-52-5
CMF C45 H61 N5 O15

Absolute stereochemistry.

PAGE 1-A



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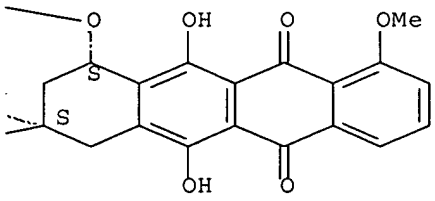
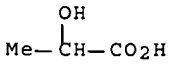


CM 2

CRN 50-21-5
CMF C3 H6 O3



RN 274913-03-0 HCAPLUS
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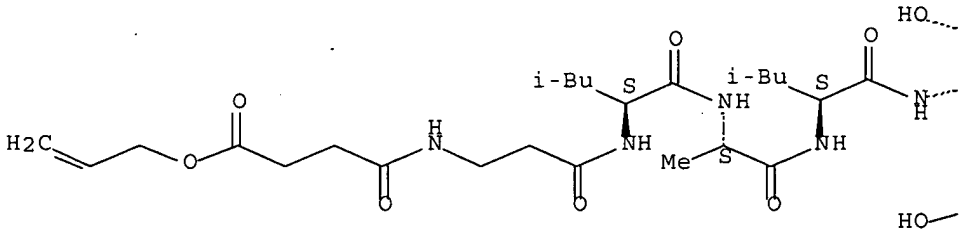
propenyloxy)butyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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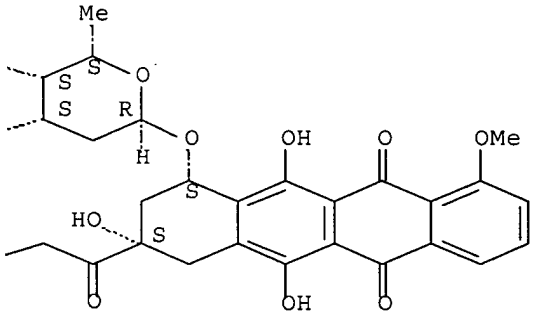
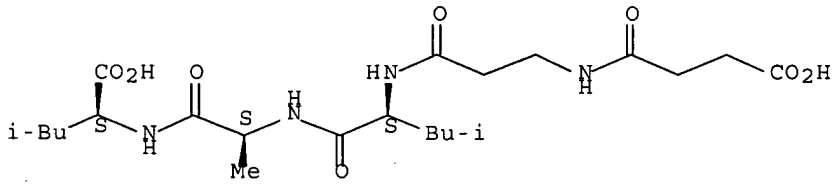


RN 274913-04-1 HCAPLUS

CN L-Leucine, N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

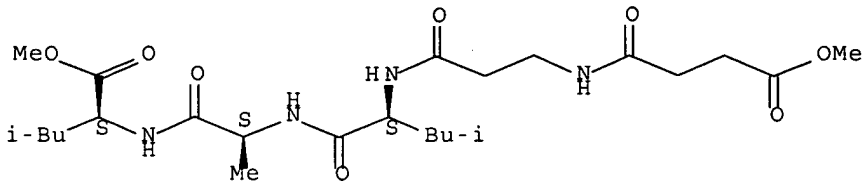
Absolute stereochemistry.



RN 274913-05-2 HCAPLUS

CN L-Leucine, N-(4-methoxy-1,4-dioxobutyl)-β-alanyl-L-leucyl-L-alanyl-, methyl ester (9CI) (CA INDEX NAME)

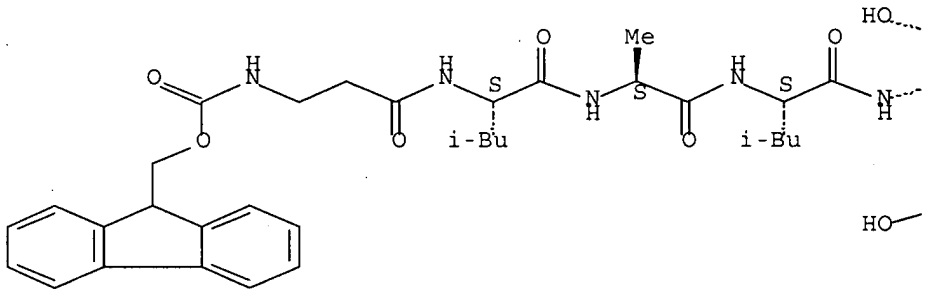
Absolute stereochemistry.



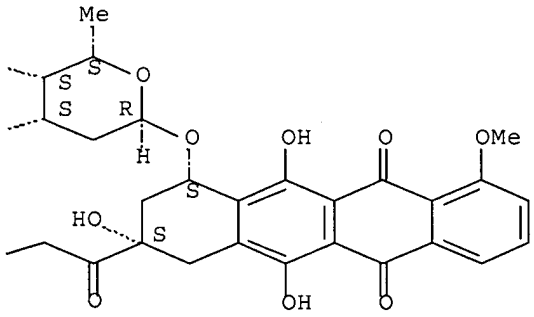
RN 274913-06-3 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



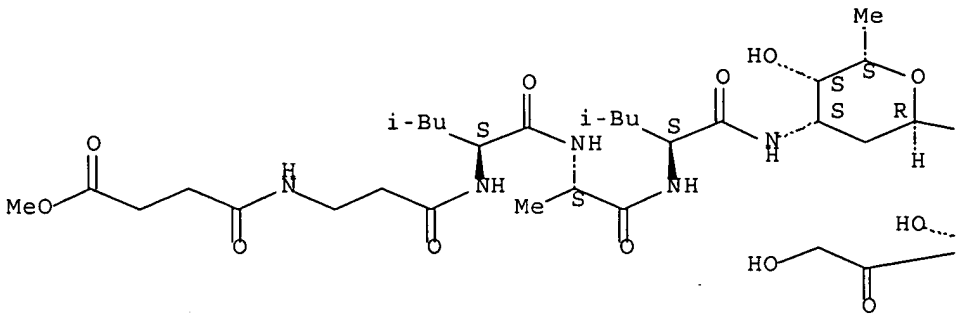
PAGE 1-B



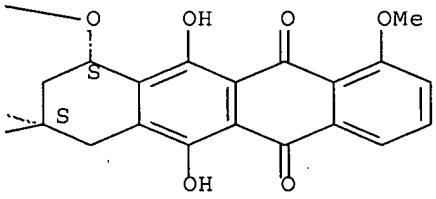
RN 274913-07-4 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-(4-methoxy-1,4-dioxobutyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 177953-71-8P 274911-87-4P 274911-89-6P
274911-90-9P 274911-91-0P 274911-93-2P
274911-94-3P 274911-96-5P 274911-98-7P
274912-01-5P 274912-03-7P 274912-05-9P
274912-06-0P 274912-08-2P 274912-09-3P
274912-12-8P 274912-13-9P 274912-15-1P
274912-17-3P 274912-19-5P 274912-20-8P
274912-34-4P 274912-35-5P 274912-36-6P
274912-39-9P 274912-44-6P 274912-47-9P
274912-49-1P 274912-50-4P 274912-52-6P
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274912-79-7P 274912-82-2P 274912-86-6P
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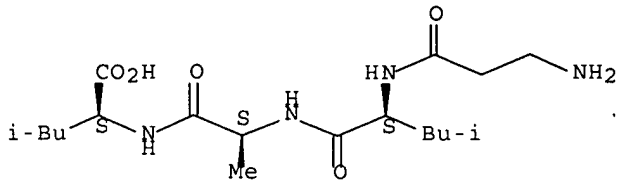
381232-63-9P 381232-64-0P 381232-71-9P
381232-73-1P 381232-74-2P 381232-75-3P
RL: PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thimet oligopeptidase-cleavable prodrug compds.)

RN 177953-71-8 HCAPLUS

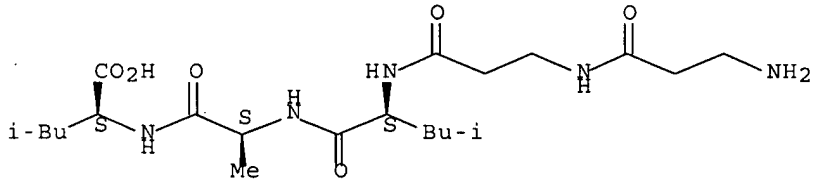
CN L-Leucine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



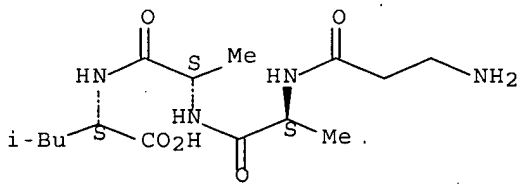
RN 274911-87-4 HCAPLUS
CN L-Leucine, β-alanyl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



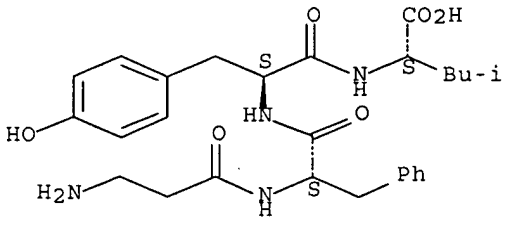
RN 274911-89-6 HCAPLUS
CN L-Leucine, β-alanyl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



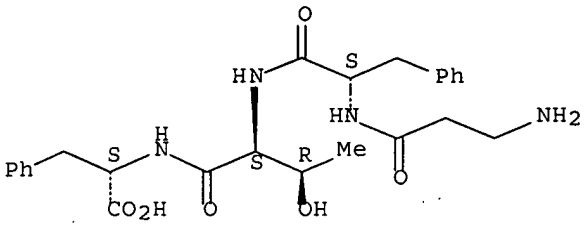
RN 274911-90-9 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



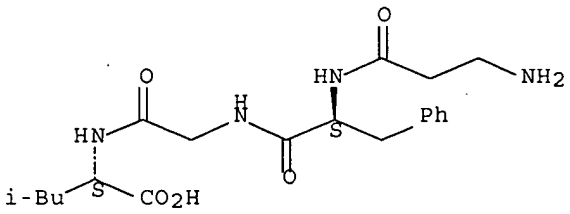
RN 274911-91-0 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-phenylalanyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



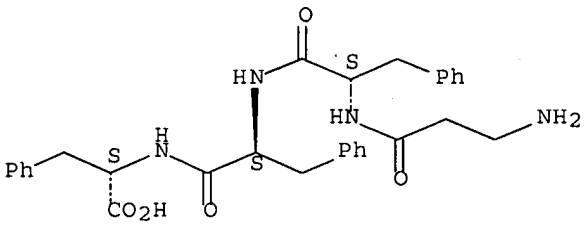
RN 274911-93-2 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



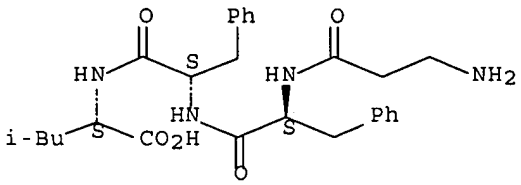
RN 274911-94-3 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



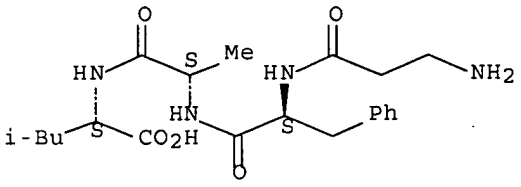
RN 274911-96-5 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



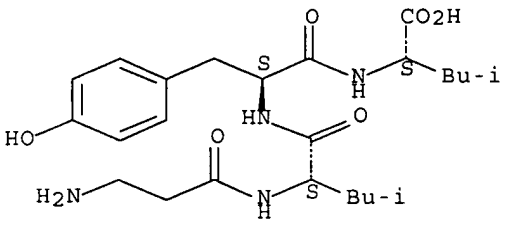
RN 274911-98-7 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



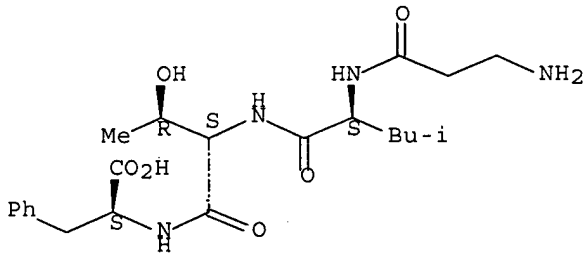
RN 274912-01-5 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



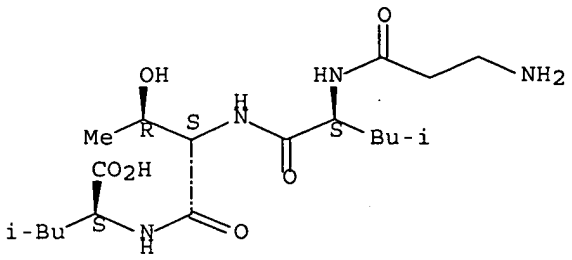
RN 274912-03-7 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-leucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



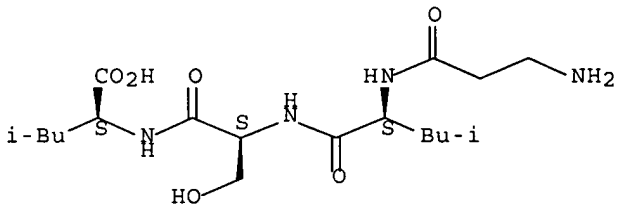
RN 274912-05-9 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



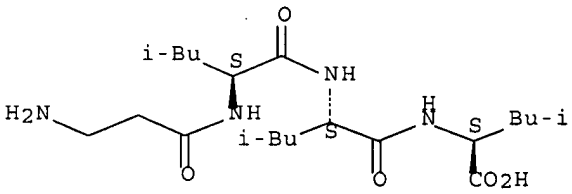
RN 274912-06-0 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



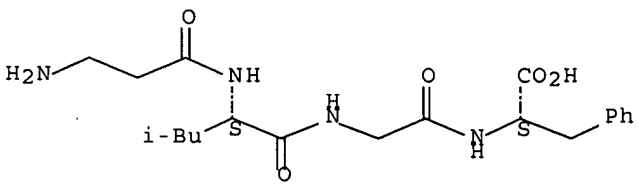
RN 274912-08-2 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274912-09-3 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-leucylglycyl- (9CI) (CA INDEX NAME)

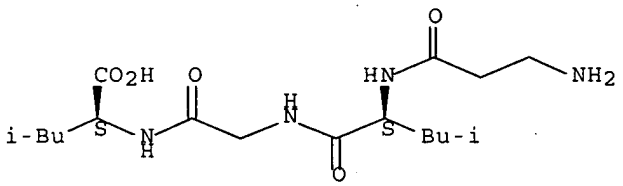
Absolute stereochemistry.



RN 274912-12-8 HCAPLUS

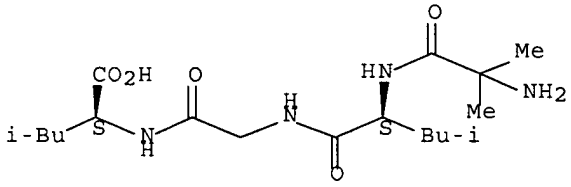
CN L-Leucine, β-alanyl-L-leucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



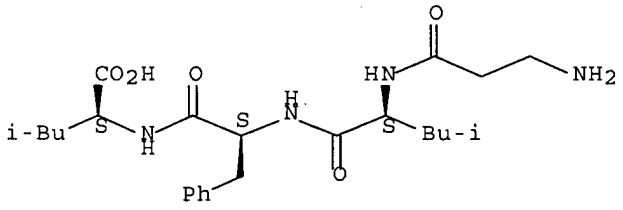
RN 274912-13-9 HCAPLUS
CN L-Leucine, 2-methylalanyl-L-leucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



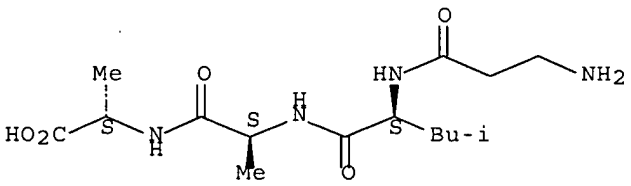
RN 274912-15-1 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



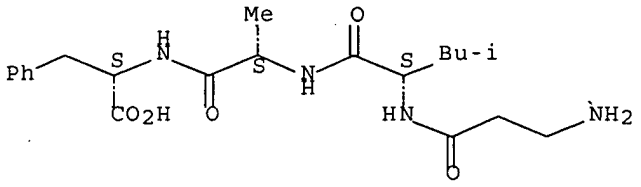
RN 274912-17-3 HCAPLUS
CN L-Alanine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



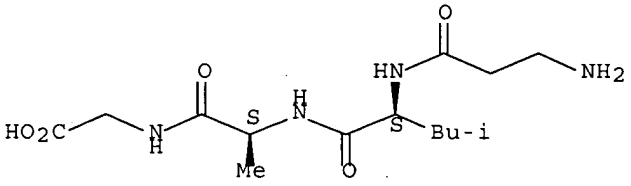
RN 274912-19-5 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



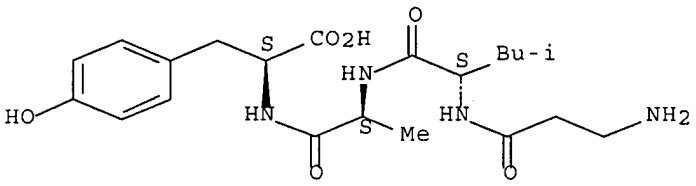
RN 274912-20-8 HCAPLUS
CN Glycine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



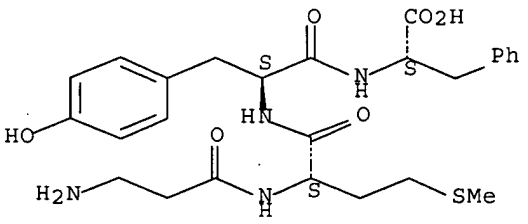
RN 274912-34-4 HCAPLUS
CN L-Tyrosine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



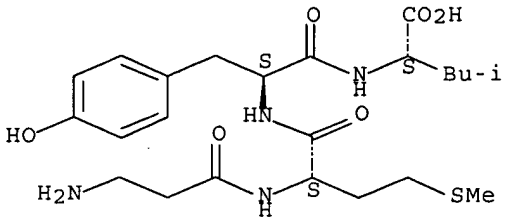
RN 274912-35-5 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-methionyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



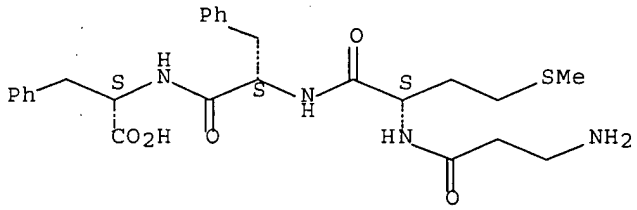
RN 274912-36-6 HCAPLUS
CN L-Leucine, β-alanyl-L-methionyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



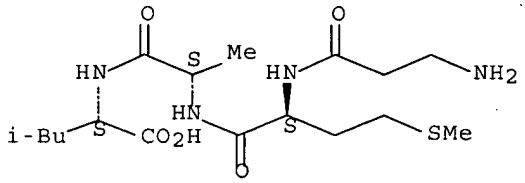
RN 274912-39-9 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-methionyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



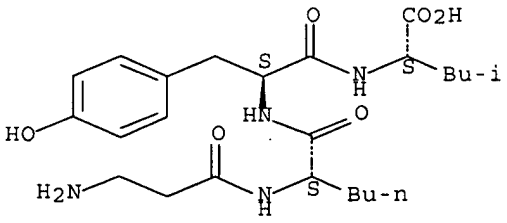
RN 274912-44-6 HCAPLUS
CN L-Leucine, β-alanyl-L-methionyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



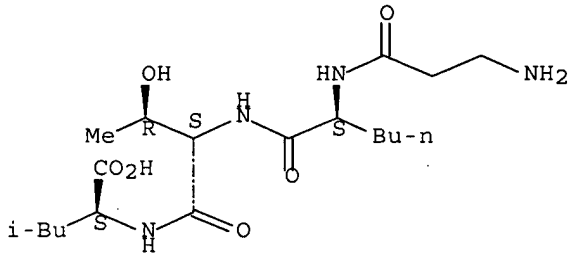
RN 274912-47-9 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



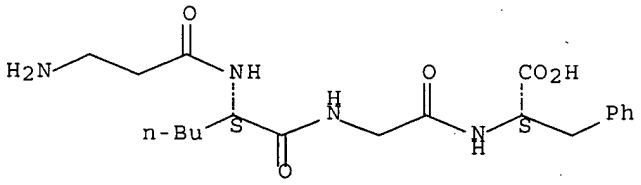
RN 274912-49-1 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



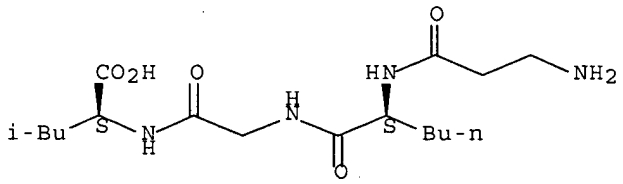
RN 274912-50-4 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-norleucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



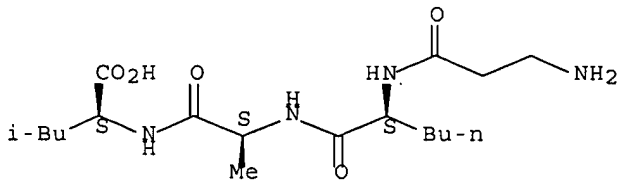
RN 274912-52-6 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



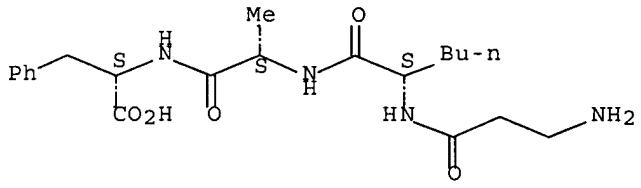
RN 274912-55-9 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



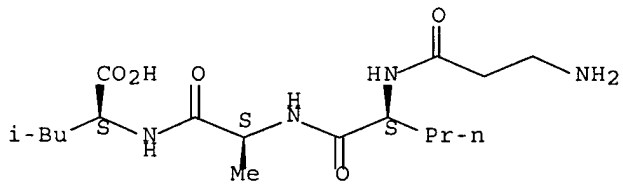
RN 274912-56-0 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-norleucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



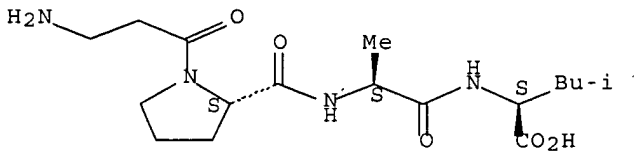
RN 274912-57-1 HCAPLUS
CN L-Leucine, β-alanyl-L-norvalyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



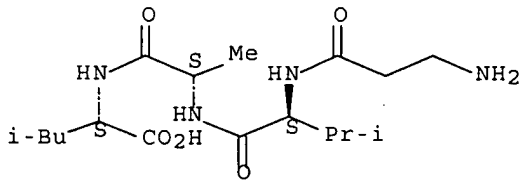
RN 274912-62-8 HCAPLUS
CN L-Leucine, β-alanyl-L-prolyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



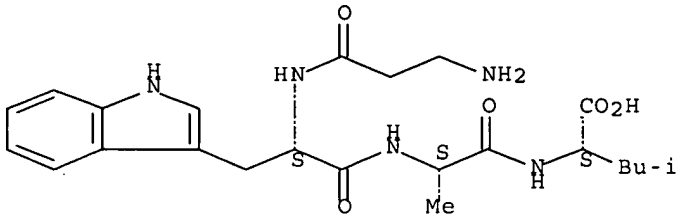
RN 274912-73-1 HCAPLUS
CN L-Leucine, β-alanyl-L-valyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



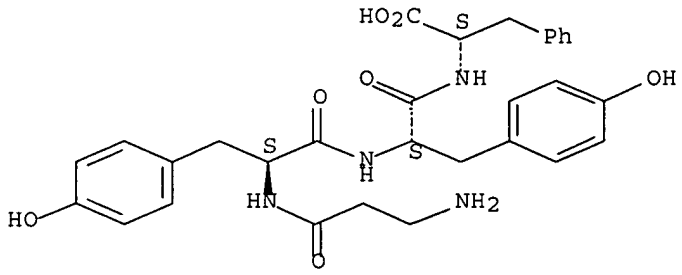
RN 274912-74-2 HCAPLUS
CN L-Leucine, β-alanyl-L-tryptophyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



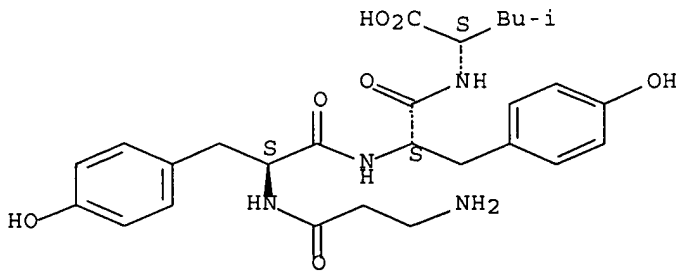
RN 274912-75-3 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-tyrosyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



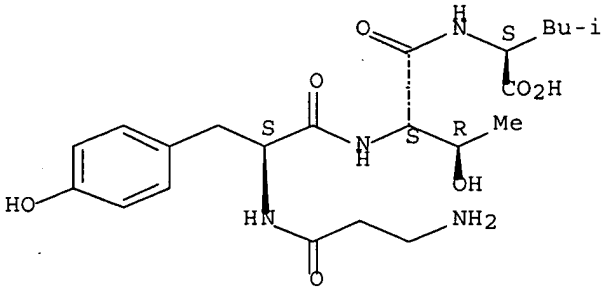
RN 274912-77-5 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



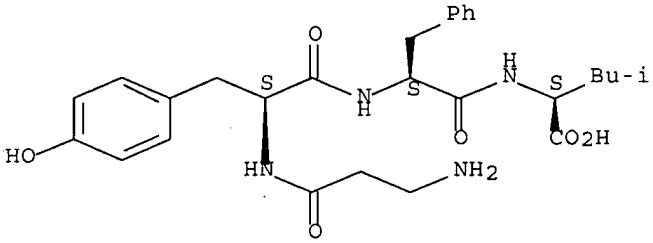
RN 274912-78-6 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



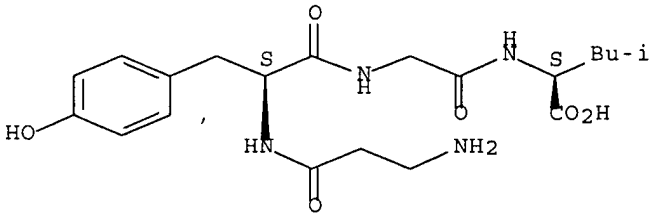
RN 274912-79-7 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



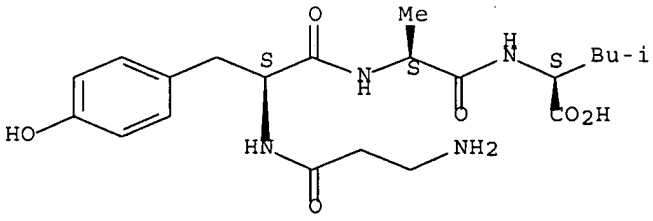
RN 274912-82-2 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274912-86-6 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-alanyl- (9CI) (CA INDEX NAME)

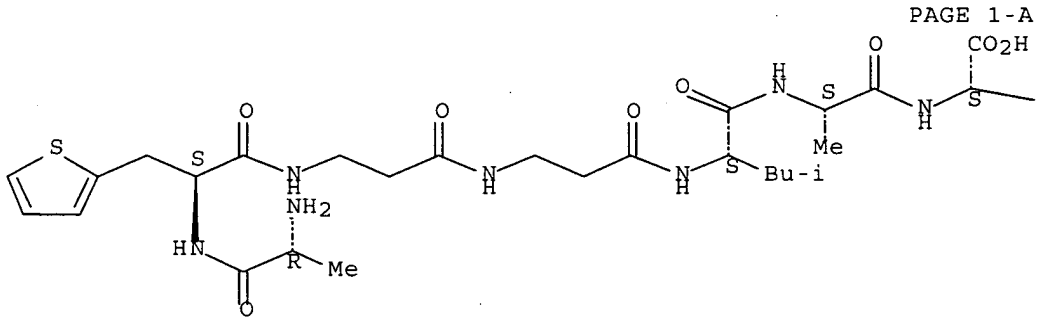
Absolute stereochemistry.



RN 381232-52-6 HCAPLUS

CN L-Leucine, D-alanyl-3-(2-thienyl)-L-alanyl-β-alanyl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

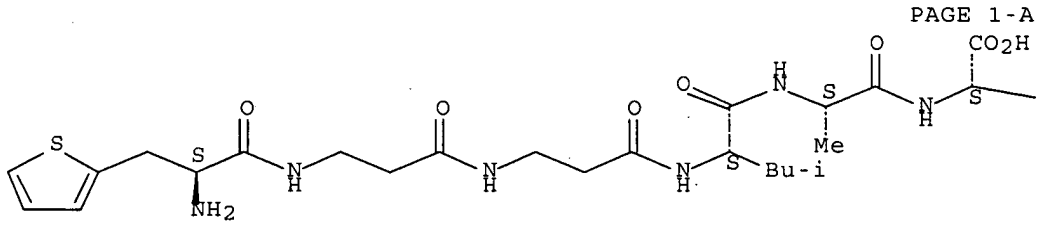
Absolute stereochemistry.



RN 381232-53-7 HCAPLUS

CN L-Leucine, 3-(2-thienyl)-L-alanyl-β-alanyl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

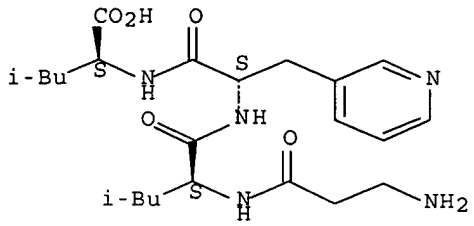
Absolute stereochemistry.



RN 381232-57-1 HCAPLUS

CN L-Leucine, β-alanyl-L-leucyl-3-(3-pyridinyl)-L-alanyl- (9CI) (CA INDEX NAME)

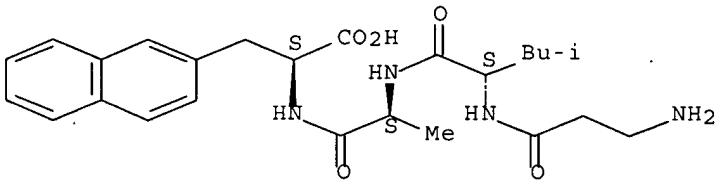
Absolute stereochemistry.



RN 381232-63-9 HCAPLUS

CN L-Alanine, β-alanyl-L-leucyl-L-alanyl-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

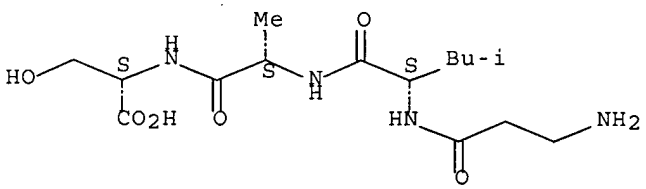
Absolute stereochemistry.



RN 381232-64-0 HCAPLUS

CN L-Serine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

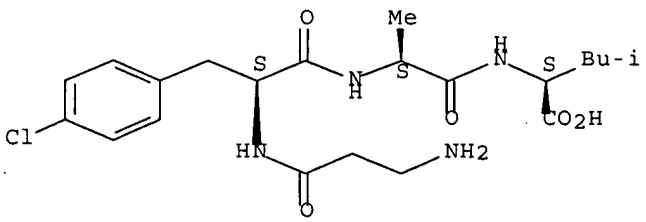
Absolute stereochemistry.



RN 381232-71-9 HCAPLUS

CN L-Leucine, β-alanyl-4-chloro-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

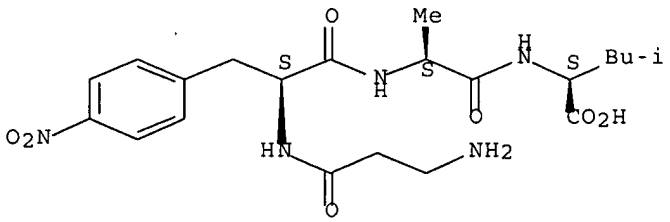
Absolute stereochemistry.



RN 381232-73-1 HCAPLUS

CN L-Leucine, β-alanyl-4-nitro-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

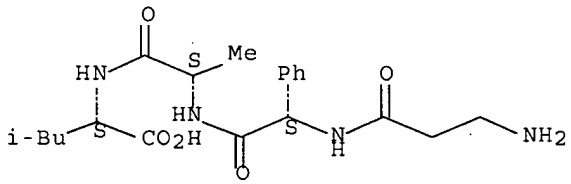
Absolute stereochemistry.



RN 381232-74-2 HCAPLUS

CN L-Leucine, β-alanyl-(2S)-2-phenylglycyl-L-alanyl- (9CI) (CA INDEX NAME)

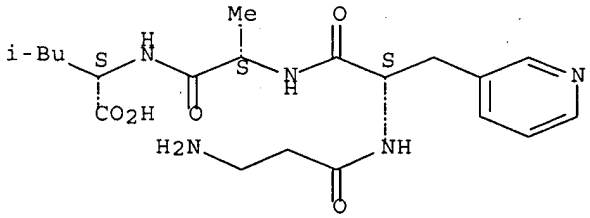
Absolute stereochemistry.



RN 381232-75-3 HCAPLUS

CN L-Leucine, β-alanyl-3-(3-pyridinyl)-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:10314 HCAPLUS Full-text

DOCUMENT NUMBER: 136:86054

TITLE: Tripeptide prodrug compounds

INVENTOR(S): Bebbington, Christopher R.; Dubois, Vincent; Gangwar, Sanjeev; Lobl, Thomas J.; Nieder, Matthew H.; Pickford, Leslie B.; Trouet, Andre; Yarranton, Geoffrey T.

PATENT ASSIGNEE(S): Corixa Corporation, USA

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002000263	A2	20020103	WO 2001-US40925		20010611
WO 2002000263	A3	20020815			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2411545	AA	20020103	CA 2001-2411545		20010611
EP 1294403	A2	20030326	EP 2001-942249		20010611
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JP 2004501875	T2	20040122	JP 2002-505044		20010611
US 2003181359	A1	20030925	US 2002-311519		20021213
PRIORITY APPLN. INFO.:			US 2000-212880P	P	20000614
			WO 2001-US40925	W	20010611

OTHER SOURCE(S): CASREACT 136:86054; MARPAT 136:86054

AB The prodrug of the invention is a modified form of a **therapeutic** agent and comprises a **therapeutic** agent, an oligopeptide AA3-AA2-AA1 (AA1 is leucine, phenylalanine, isoleucine, alanine, glycine, tyrosine, 2-naphthylalanine, or serine; AA2 is alanine, leucine, tyrosine, glycine, serine, 3-pyridylalanine, 2-thienylalanine, aminoisobutyric acid, threonine, or phenylalanine; AA3 is leucine, sarcosine, tyrosine, phenylalanine, p-chloro- or p-nitrophenylalanine, valine, norleucine, norvaline, phenylglycine, tryptophan, tetrahydroisoquinoline-3-carboxylic acid, 3-pyridylalanine, alanine, glycine, 2-thienylalanine, methionine, or proline), a stabilizing group and, optionally, a linker group. The prodrug is cleavable by a trouase enzyme such as Thimet oligopeptidase. Thus, Suc-Leu-Ala-Leu-Dox (Suc = succinic acid residue, Dox = doxorubicin residue), prepared by conjugation of doxorubicin hydrochloride with Fmoc-Leu-Ala-Leu-OH, deprotection, and acylation with succinic anhydride, showed tumor-activated prodrug activity on LNCaP, HT-29 and PC-3 cells of 0.016, 0.052, and 0.075 μM, resp. Suc-Leu-Ala-Leu-Dox is better tolerated in vivo than is doxorubicin.

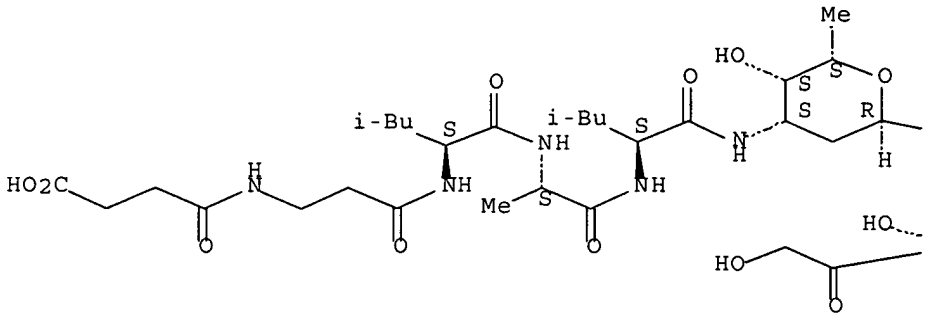
IT **274912-87-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tripeptide prodrug compds.)

RN 274912-87-7 HCAPLUS

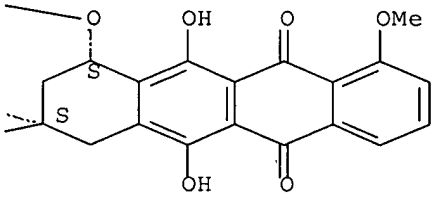
CN 5,12-Naphthacenedione, 10-[[3-[[N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L7 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:923644 HCAPLUS Full-text
DOCUMENT NUMBER: 136:58787
TITLE: Enzyme-cleavable prodrug compounds
INVENTOR(S): Nieder, Matthew H.; Dubois, Vincent; Gangwar, Sanjeev; Lobl, Thomas J.; Pickford, Leslie B.; Trouet, Andre; Yarranton, Geoffrey T.
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095945	A2	20011220	WO 2001-US18903	20010611
WO 2001095945	A3	20020815		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2411660	AA	20011220	CA 2001-2411660	20010611
EP 1294405	A2	20030326	EP 2001-950291	20010611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004510703	T2	20040408	JP 2002-510122	20010611
PRIORITY APPLN. INFO.:			US 2000-211887P	P 20000614
			US 2001-290448P	P 20010511
			WO 2001-US18903	W 20010611

OTHER SOURCE(S): MARPAT 136:58787

AB The prodrug of the invention is a modified form of a **therapeutic** agent and comprises a **therapeutic** agent, an oligopeptide, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by the enzyme, thimet oligopeptidase (TOP). Also disclosed are methods of designing prodrugs by utilizing TOP-cleavage sequences within the **conjugate** and methods of treating patients with prodrugs of the invention.

IT 177953-71-8DP, drug **conjugates** 274911-87-4DP, drug **conjugates** 274911-89-6DP, drug **conjugates** 274911-90-9DP, drug **conjugates** 274911-91-0DP, drug **conjugates** 274911-93-2DP, drug **conjugates** 274911-94-3DP, drug **conjugates** 274911-96-5DP, drug **conjugates** 274911-98-7DP, drug **conjugates** 274912-01-5DP, drug **conjugates** 274912-03-7DP, drug **conjugates** 274912-05-9DP, drug **conjugates** 274912-06-0DP, drug **conjugates** 274912-08-2DP, drug **conjugates** 274912-09-3DP, drug **conjugates** 274912-12-8DP, drug **conjugates** 274912-13-9DP, drug **conjugates** 274912-15-1DP, drug **conjugates** 274912-17-3DP, drug **conjugates** 274912-19-5DP, drug **conjugates** 274912-20-8DP, drug **conjugates** 274912-34-4DP, drug **conjugates** 274912-35-5DP, drug **conjugates** 274912-36-6DP, drug **conjugates** 274912-39-9DP, drug **conjugates** 274912-44-6DP, drug **conjugates** 274912-47-9DP, drug **conjugates** 274912-49-1DP, drug **conjugates** 274912-50-4DP, drug **conjugates** 274912-52-6DP, drug **conjugates** 274912-55-9DP, drug **conjugates** 274912-56-0DP, drug **conjugates** 274912-57-1DP, drug **conjugates** 274912-62-8DP, drug **conjugates** 274912-73-1DP, drug **conjugates** 274912-74-2DP, drug **conjugates** 274912-75-3DP, drug **conjugates** 274912-77-5DP, drug **conjugates** 274912-78-6DP, drug **conjugates** 274912-79-7DP, drug **conjugates** 274912-82-2DP, drug **conjugates** 274912-86-6DP, drug **conjugates** 274912-87-7P 274912-88-8P 274912-89-9P 381232-52-6DP, drug **conjugates** 381232-53-7DP, drug **conjugates** 381232-57-1DP, drug **conjugates** 381232-63-9DP, drug **conjugates** 381232-64-0DP, drug **conjugates** 381232-71-9DP, drug **conjugates** 381232-73-1DP, drug **conjugates** 381232-74-2DP, drug **conjugates** 381232-75-3DP, drug **conjugates**

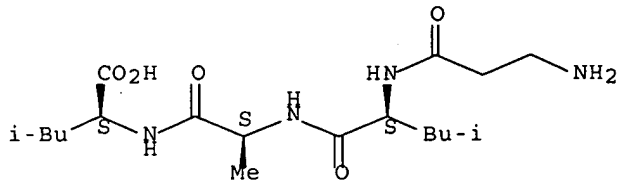
RL: PAC (Pharmacological activity); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(enzyme-cleavable prodrug compds.)

RN 177953-71-8 HCAPLUS

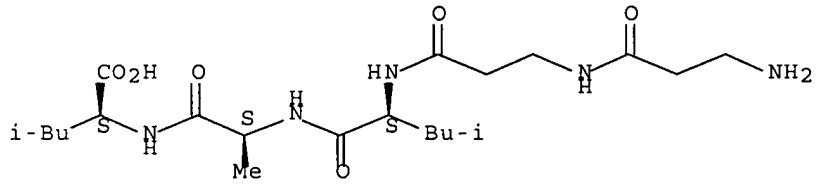
CN L-Leucine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



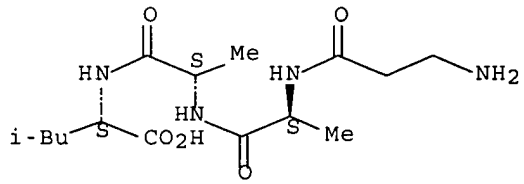
RN 274911-87-4 HCAPLUS
CN L-Leucine, β-alanyl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



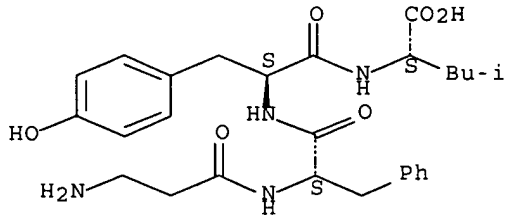
RN 274911-89-6 HCAPLUS
CN L-Leucine, β-alanyl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



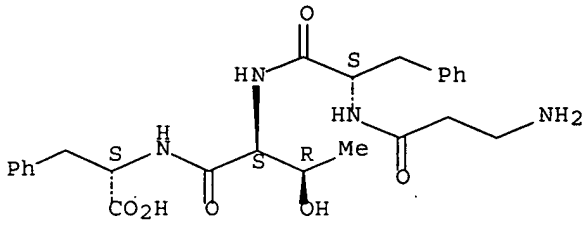
RN 274911-90-9 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



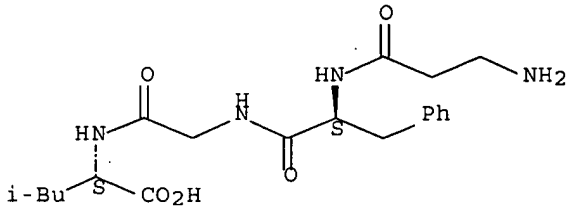
RN 274911-91-0 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-phenylalanyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



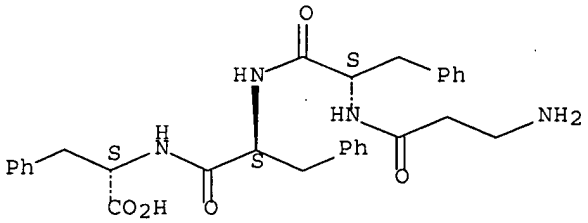
RN 274911-93-2 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



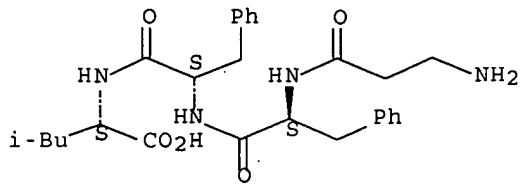
RN 274911-94-3 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



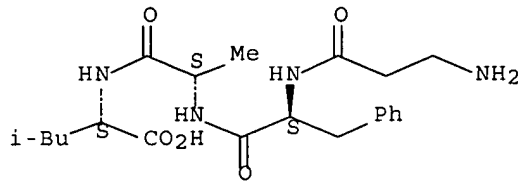
RN 274911-96-5 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



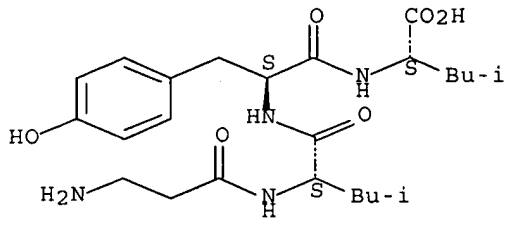
RN 274911-98-7 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



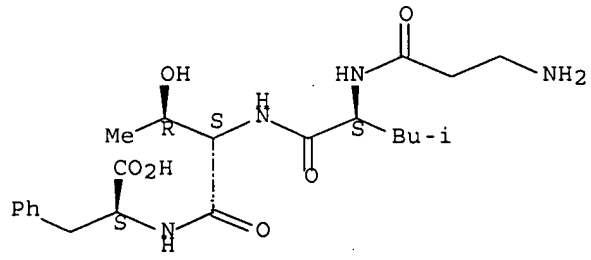
RN 274912-01-5 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



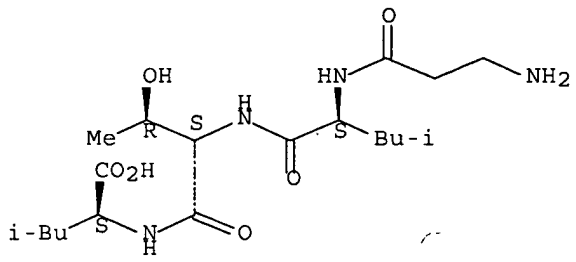
RN 274912-03-7 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-leucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



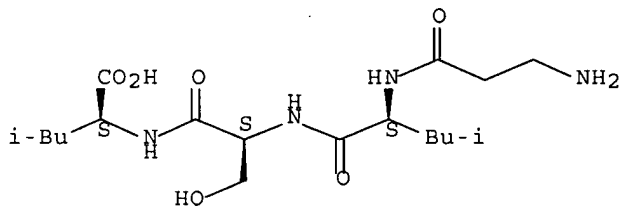
RN 274912-05-9 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



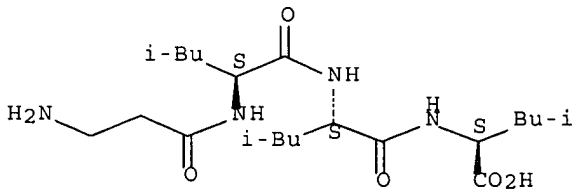
RN 274912-06-0 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



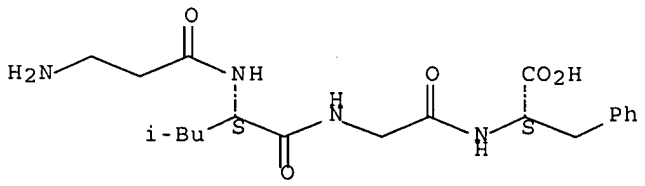
RN 274912-08-2 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



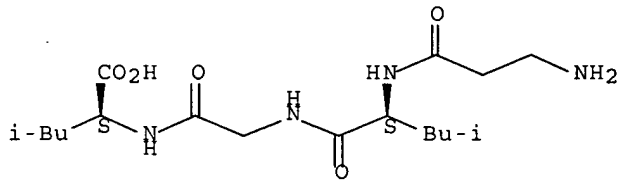
RN 274912-09-3 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-leucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



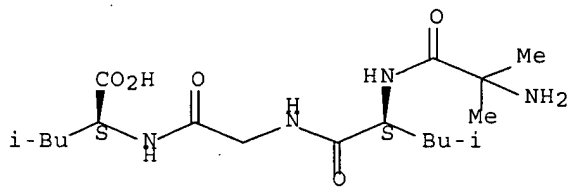
RN 274912-12-8 HCAPLUS
CN L-Leucine, β-alanyl-L-leucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



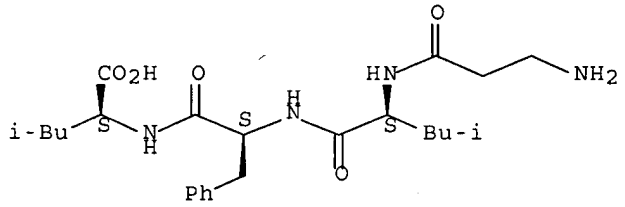
RN 274912-13-9 HCAPLUS
CN L-Leucine, 2-methylalanyl-L-leucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



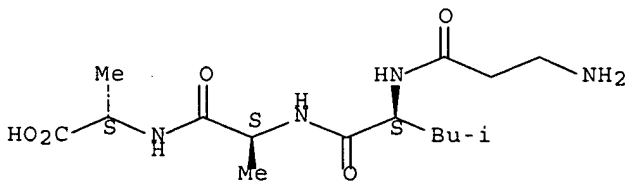
RN 274912-15-1 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



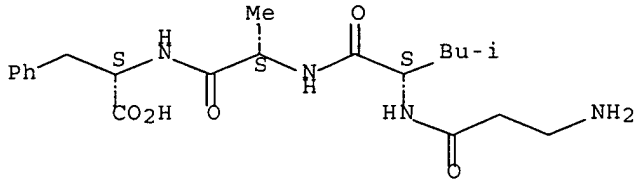
RN 274912-17-3 HCAPLUS
CN L-Alanine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



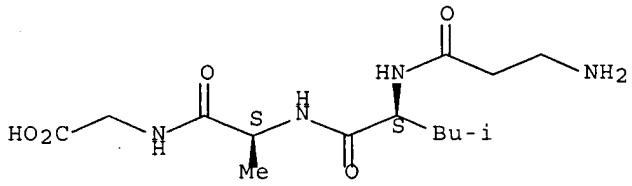
RN 274912-19-5 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



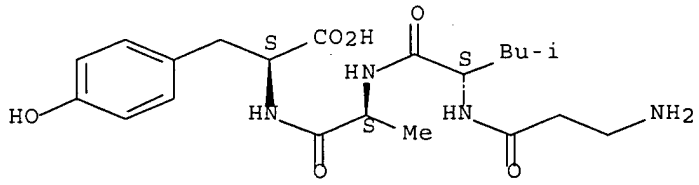
RN 274912-20-8 HCAPLUS
CN Glycine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



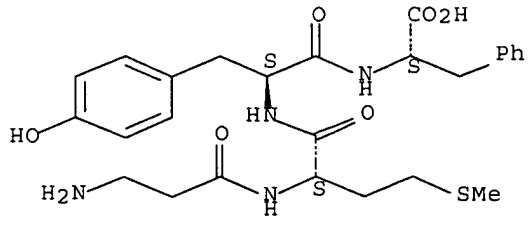
RN 274912-34-4 HCAPLUS
CN L-Tyrosine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



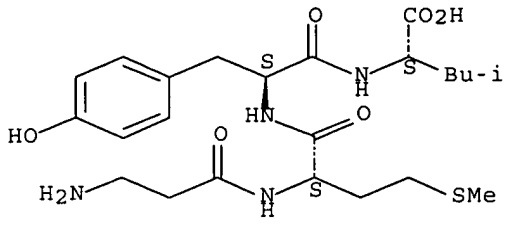
RN 274912-35-5 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-methionyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



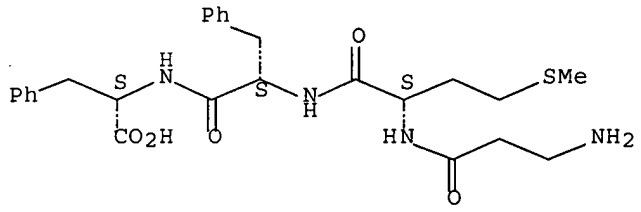
RN 274912-36-6 HCAPLUS
CN L-Leucine, β-alanyl-L-methionyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



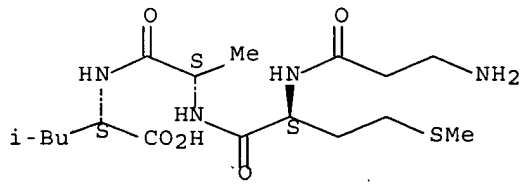
RN 274912-39-9 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-methionyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



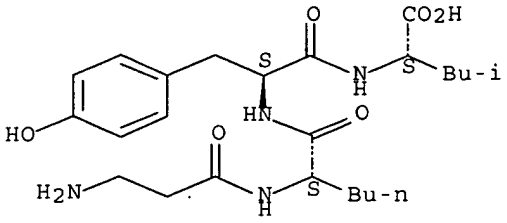
RN 274912-44-6 HCAPLUS
CN L-Leucine, β-alanyl-L-methionyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



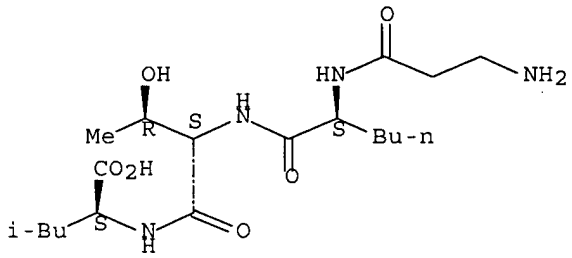
RN 274912-47-9 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



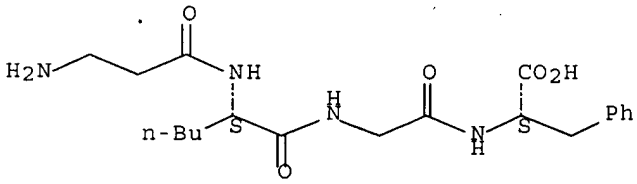
RN 274912-49-1 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



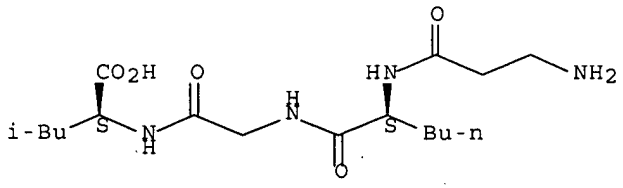
RN 274912-50-4 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-norleucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



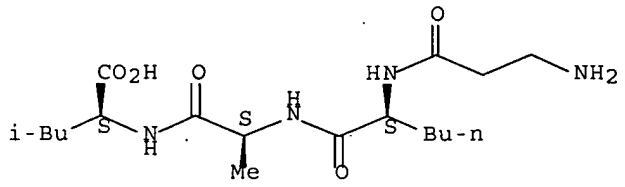
RN 274912-52-6 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



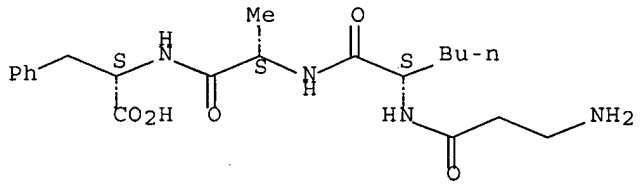
RN 274912-55-9 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



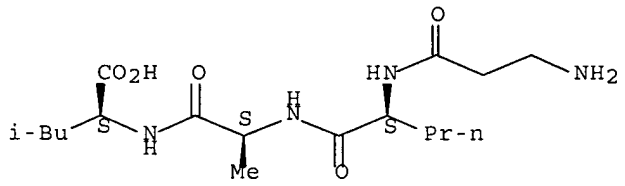
RN 274912-56-0 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-norleucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



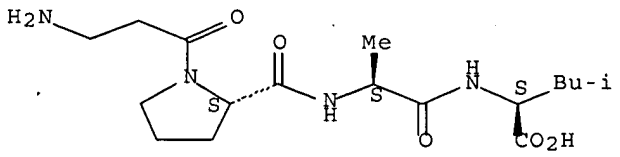
RN 274912-57-1 HCAPLUS
CN L-Leucine, β-alanyl-L-norvalyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



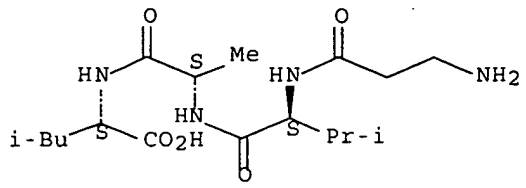
RN 274912-62-8 HCAPLUS
CN L-Leucine, β-alanyl-L-prolyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



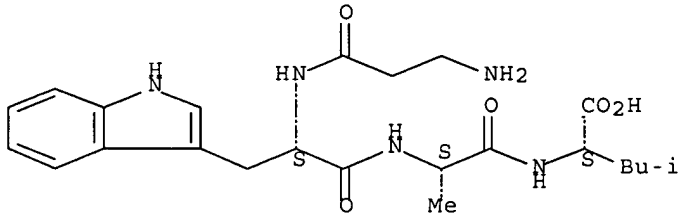
RN 274912-73-1 HCAPLUS
CN L-Leucine, β-alanyl-L-valyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



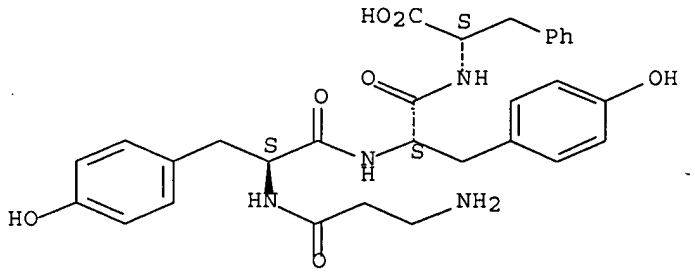
RN 274912-74-2 HCAPLUS
CN L-Leucine, β-alanyl-L-tryptophyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



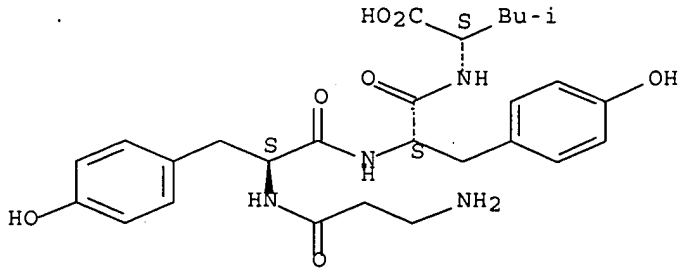
RN 274912-75-3 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-tyrosyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



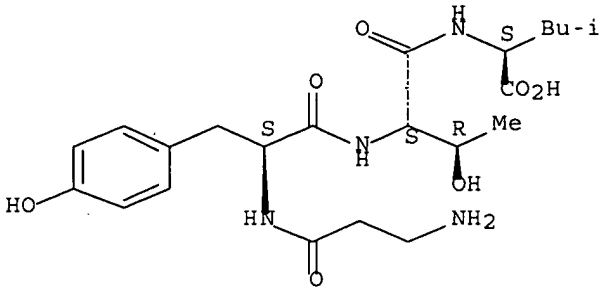
RN 274912-77-5 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



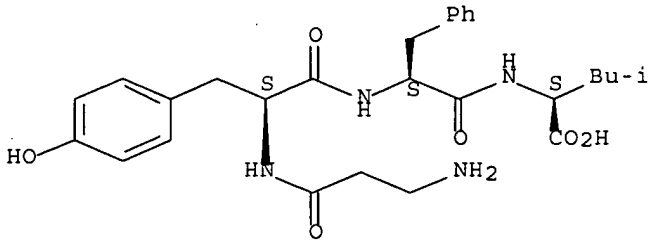
RN 274912-78-6 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



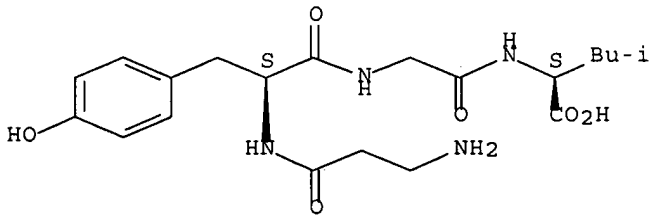
RN 274912-79-7 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



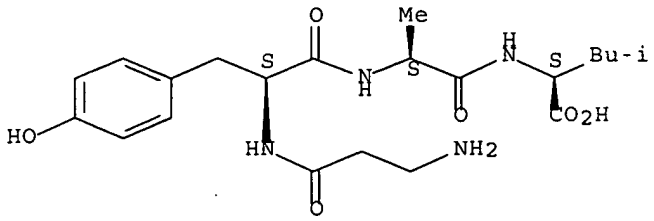
RN 274912-82-2 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274912-86-6 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

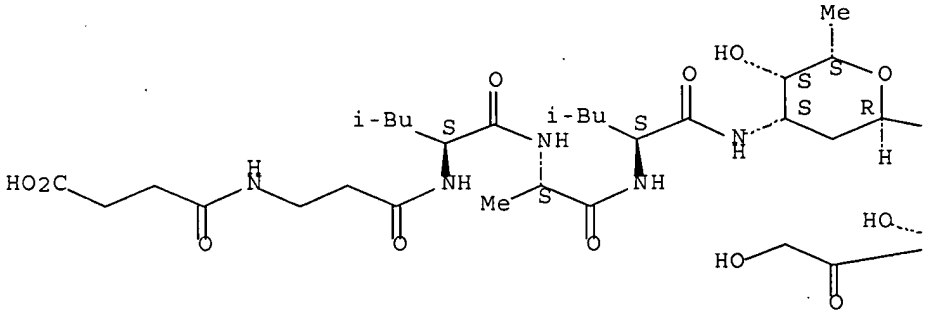


RN 274912-87-7 HCAPLUS

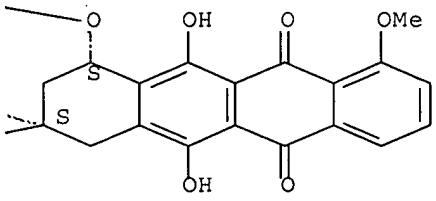
CN 5,12-Naphthacenedione, 10-[[3-[[N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

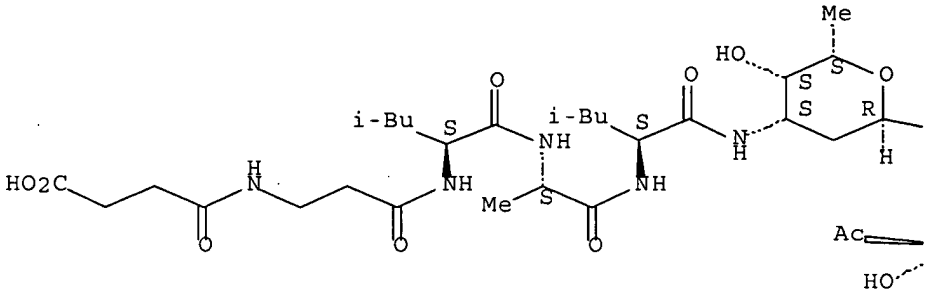


RN 274912-88-8 HCAPLUS

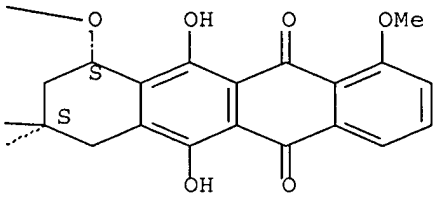
CN 5,12-Naphthacenedione, 8-acetyl-10-[[3-[[N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

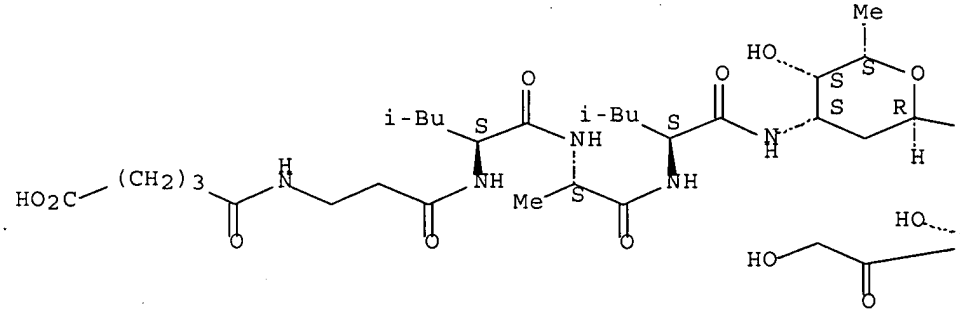


RN 274912-89-9 HCAPLUS

CN 5,12-Naphthacenedione, 10-[[3-[[N-(4-carboxy-1-oxobutyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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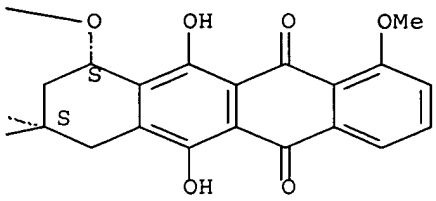
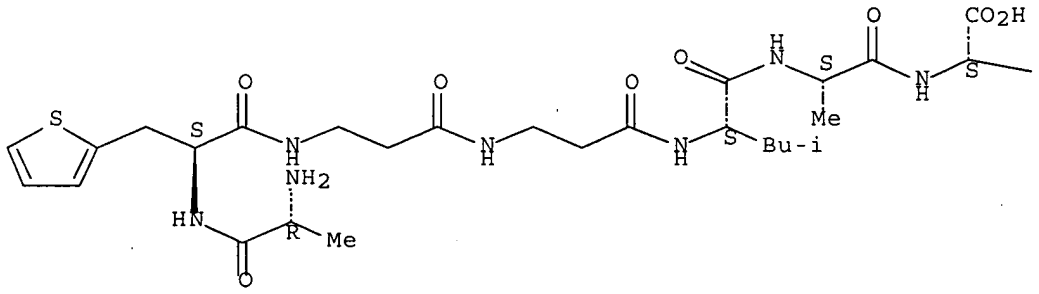


RN 381232-52-6 HCAPLUS

CN L-Leucine, D-alanyl-3-(2-thienyl)-L-alanyl-β-alanyl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

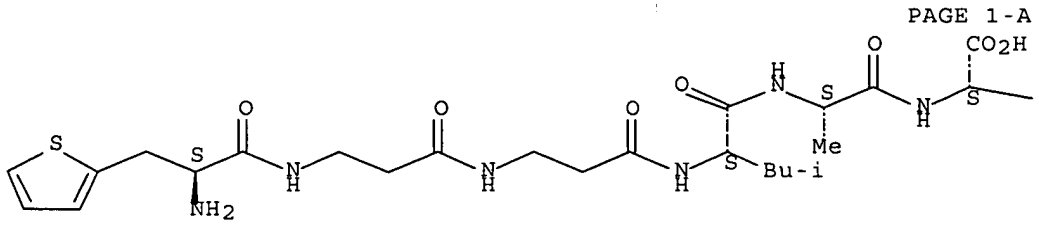
—Bu-i

RN 381232-53-7 HCAPLUS

CN L-Leucine, 3-(2-thienyl)-L-alanyl-β-alanyl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

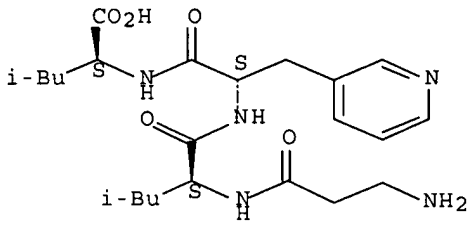
PAGE 1-A



—Bu-i

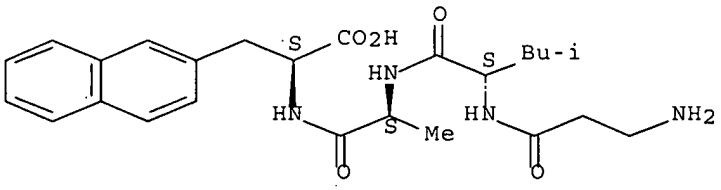
RN 381232-57-1 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-3-(3-pyridinyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



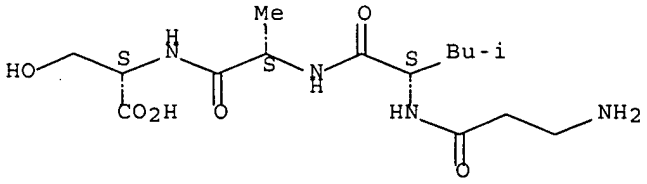
RN 381232-63-9 HCAPLUS
CN L-Alanine, β-alanyl-L-leucyl-L-alanyl-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



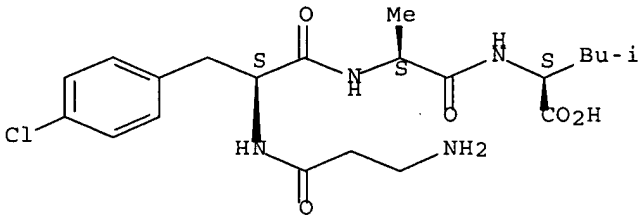
RN 381232-64-0 HCAPLUS
CN L-Serine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 381232-71-9 HCAPLUS
CN L-Leucine, β-alanyl-4-chloro-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

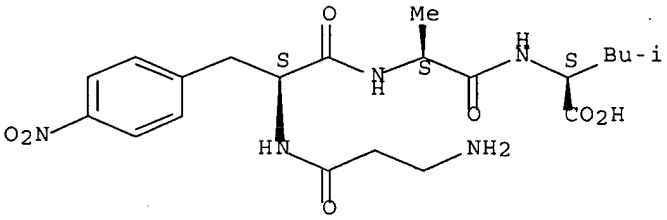
Absolute stereochemistry.



RN 381232-73-1 HCAPLUS

CN L-Leucine, β-alanyl-4-nitro-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

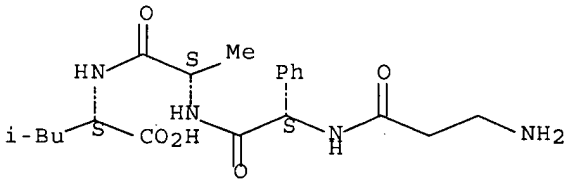
Absolute stereochemistry.



RN 381232-74-2 HCAPLUS

CN L-Leucine, β-alanyl-(2S)-2-phenylglycyl-L-alanyl- (9CI) (CA INDEX NAME)

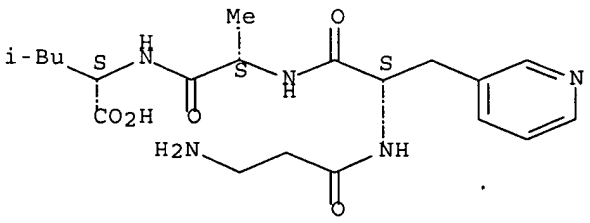
Absolute stereochemistry.



RN 381232-75-3 HCAPLUS

CN L-Leucine, β-alanyl-3-(3-pyridinyl)-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:693138 HCAPLUS Full-text
DOCUMENT NUMBER: 135:273218
TITLE: Preparation of peptidase-cleavable, targeted antineoplastic drugs and their **therapeutic** use
INVENTOR(S): Copeland, Robert A.; Albright, Charles F.; Combs, Andrew P.; Dowling, Radine L.; Graciani, Nilsa R.; Han, Wei; Higley, C. Anne; Huang, Pearl S.; Yue, Eddy W.; Dimeo, Susan V.
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 203 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001068145	A2	20010920	WO 2001-US8589		20010315
WO 2001068145	A3	20020711			
W: AT, AU, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HU, IN, JP, KR, LT, LU, LV, MX, NZ, PL, PT, RO, RU, SE, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR					
CA 2401873	AA	20010920	CA 2001-2401873		20010315
US 2002103133	A1	20020801	US 2001-808832		20010315
US 6844318	B2	20050118			
EP 1263473	A2	20021211	EP 2001-918798		20010315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, CY, TR					
BR 2001009266	A	20030429	BR 2001-9266		20010315
JP 2003526683	T2	20030909	JP 2001-566708		20010315
EE 200200522	A	20040415	EE 2002-522		20010315
PRIORITY APPLN. INFO.:			US 2000-189387P	P	20000315
			WO 2001-US8589	W	20010315

OTHER SOURCE(S): MARPAT 135:273218

AB This invention is directed to antineoplastic agents conjugated to enzyme-cleavable peptides comprising the amino acid recognition sequence of a membrane-bound and/or cell-secreted peptidase. The conjugated compds. are for use as chemotherapeutic agents in the targeted treatment of cancers. Claimed peptide sequences include Cap-Paa-Xa2-Gly-Xp1-Laa, where Cap is an N-terminus group R, Xa4 or R-Xa4 (R is an amino capping group, Xa4 is an amino acid), Paa is Pro, 4-hydroxyproline (Hyp), 2-carboxyazetidine (Aze), homo-Pro, cyclohexylglycine (Chg), 4-fluorophenylalanine (Fph), nipecotic acid (Npa), 4-thiazolidinecarboxylic acid (Tzc), or proline mimetic; Xa2 is an amino acid; Xp1 is is an amino acid wherein -Gly-Xp1- or -Sar-Xp1 form a bond cleavable by a matrixin; Laa is an amino acid, e.g., Leu, Ile, Nle, β-homo-Leu, homoleucine, homoserine, Ala and cyclohexylalanine. Thus, peptide **conjugate** Ac-PLGLYL-Dox (Dox = doxorubicin) was prepared by the solid phase method and evaluated for stability in blood and cleavage with MMPs and neprilysin.

IT **360779-43-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

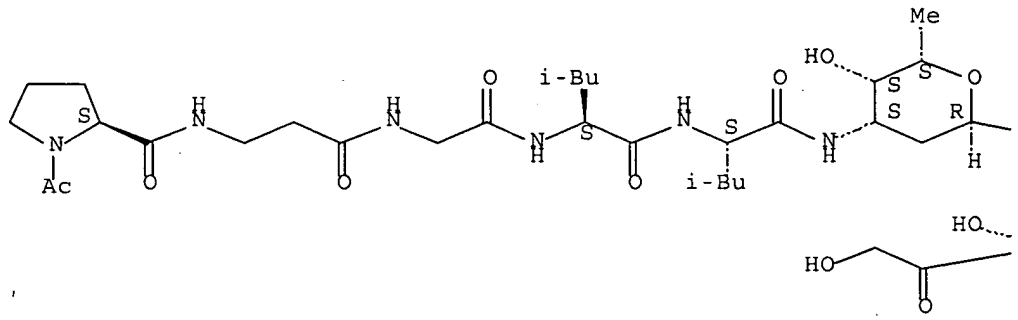
(preparation of antineoplastic agents conjugated to enzyme-cleavable peptides)

RN 360779-43-7 HCAPLUS

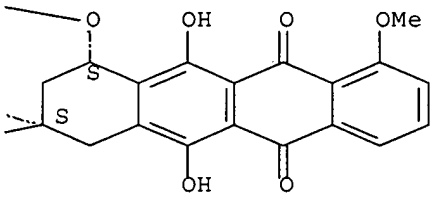
CN 5,12-Naphthacenedione, 10-[[3-[(1-acetyl-L-prolyl-β-alanylglycyl-L-leucyl-L-leucyl)amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L7 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:401690 HCAPLUS Full-text

DOCUMENT NUMBER: 133:48878

TITLE: Oligopeptide prodrug compounds and process for preparation thereof

INVENTOR(S): Lobl, Thomas J.; Dubois, Vincent; Fernandez, Anne-Marie; Gangwar, Sanjeev; Lewis, Evan; Nieder, Matthew H.; Trouet, Andre; Viski, Peter; Yarranton, Geoffrey T.

PATENT ASSIGNEE(S): Coulter Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000033888	A2	20000615	WO 1999-US30393		19991210
WO 2000033888	A3	20011108			
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2354766	AA	20000615	CA 1999-2354766		19991210
EP 1144011	A2	20011017	EP 1999-967462		19991210
EP 1144011	A3	20020206			
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JP 2003518000	T2	20030603	JP 2000-586378		19991210
AU 773420	B2	20040527	AU 2000-23733		19991210
NZ 512171	A	20040730	NZ 1999-512171		19991210
US 2002142955	A1	20021003	US 2001-879442		20010611
PRIORITY APPLN. INFO.:			US 1998-111793P	P	19981211
			US 1999-119312P	P	19990208
			WO 1999-US30393	W	19991210
			US 2000-211887P	P	20000614
			US 2001-290448P	P	20010511

OTHER SOURCE(S): MARPAT 133:48878

AB The prodrug of the invention is a modified form of a **therapeutic** agent and comprises a **therapeutic** agent, an oligopeptide, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by the enzyme trouase. Also disclosed are processes for making the prodrug compds.

IT **177953-71-8 274911-85-2 274911-86-3**
274911-87-4 274911-89-6 274911-90-9
274911-91-0 274911-93-2 274911-94-3
274911-96-5 274911-98-7 274912-01-5
274912-03-7 274912-05-9 274912-06-0
274912-07-1 274912-08-2 274912-09-3
274912-12-8 274912-13-9 274912-15-1
274912-17-3 274912-19-5 274912-20-8
274912-32-2 274912-34-4 274912-35-5
274912-36-6 274912-39-9 274912-44-6
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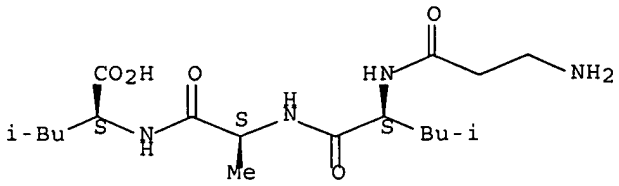
274912-57-1 274912-62-8 274912-63-9
274912-65-1 274912-66-2 274912-67-3
274912-73-1 274912-74-2 274912-75-3
274912-77-5 274912-78-6 274912-79-7
274912-82-2 274912-86-6
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(oligopeptide prodrug compds. and process for preparation thereof)

RN 177953-71-8 HCAPLUS

CN L-Leucine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

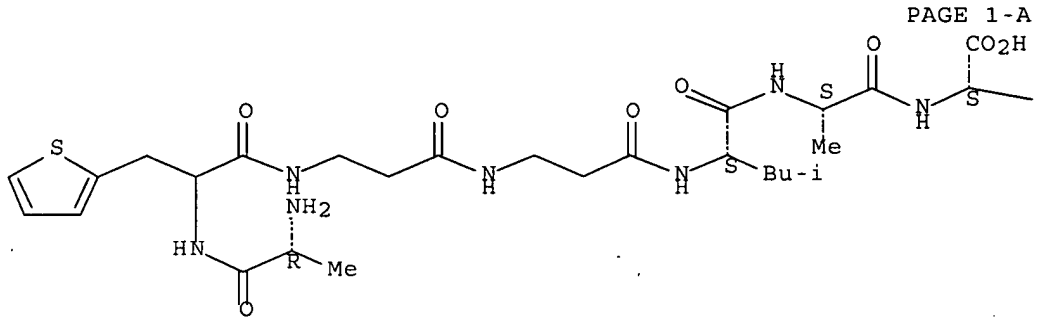


RN 274911-85-2 HCAPLUS

CN L-Leucine, D-alanyl-3-(2-thienyl)alanyl-β-alanyl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

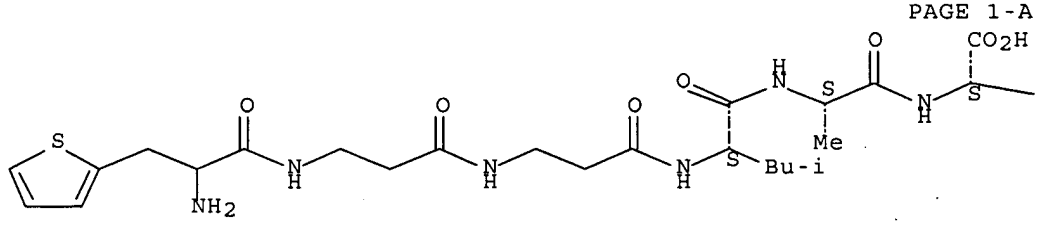
—Bu-i

RN 274911-86-3 HCAPLUS

CN L-Leucine, 3-(2-thienyl)alanyl-β-alanyl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

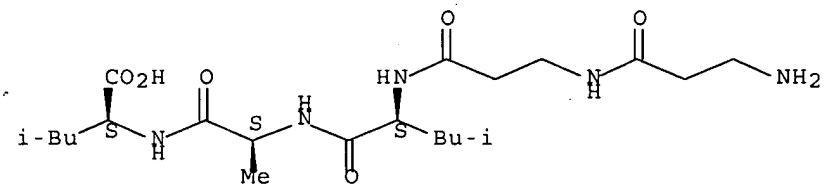
PAGE 1-A



—Bu-i

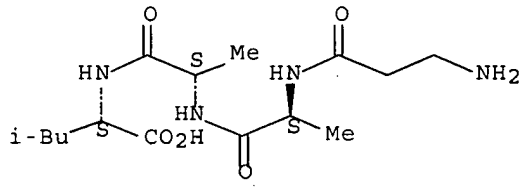
RN 274911-87-4 HCAPLUS
CN L-Leucine, β-alanyl-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



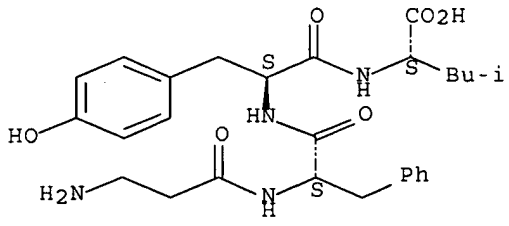
RN 274911-89-6 HCAPLUS
CN L-Leucine, β-alanyl-L-alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



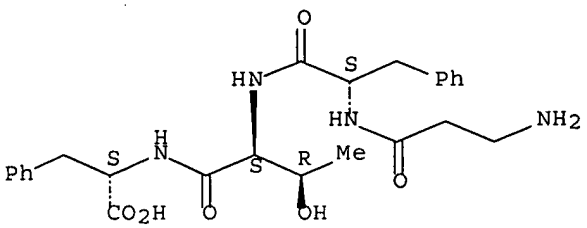
RN 274911-90-9 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274911-91-0 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-phenylalanyl-L-threonyl- (9CI) (CA INDEX NAME)

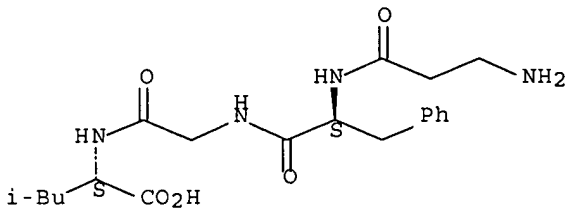
Absolute stereochemistry.



RN 274911-93-2 HCAPLUS

CN L-Leucine, β-alanyl-L-phenylalanylglycyl- (9CI) (CA INDEX NAME)

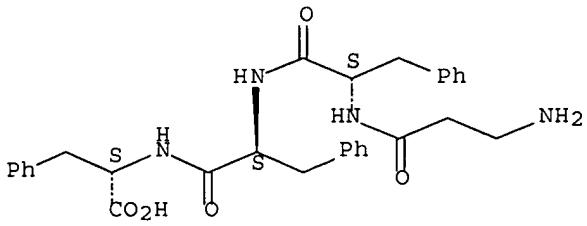
Absolute stereochemistry.



RN 274911-94-3 HCAPLUS

CN L-Phenylalanine, β-alanyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

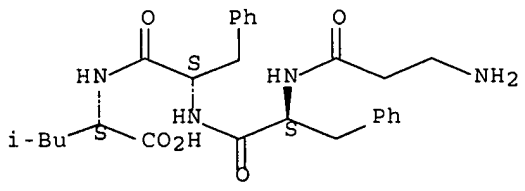
Absolute stereochemistry.



RN 274911-96-5 HCAPLUS

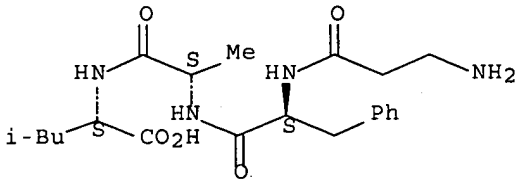
CN L-Leucine, β-alanyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



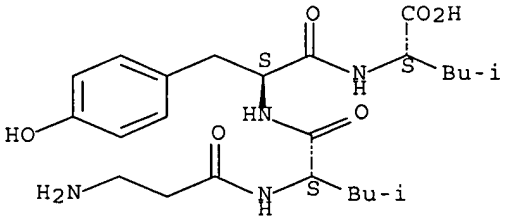
RN 274911-98-7 HCAPLUS
CN L-Leucine, β-alanyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



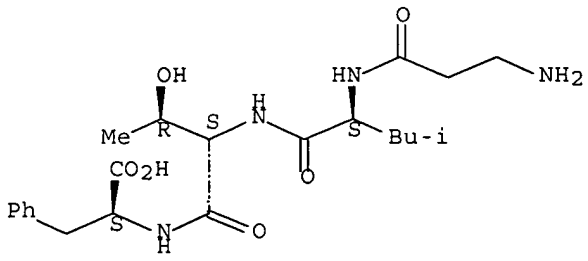
RN 274912-01-5 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



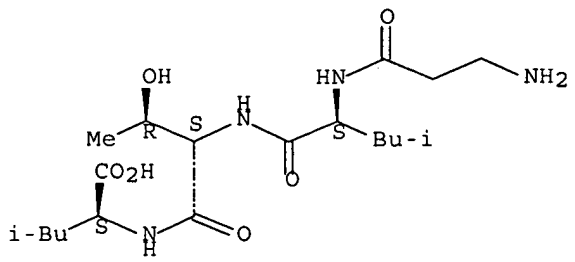
RN 274912-03-7 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-leucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



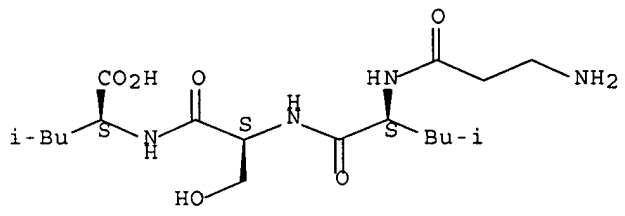
RN 274912-05-9 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



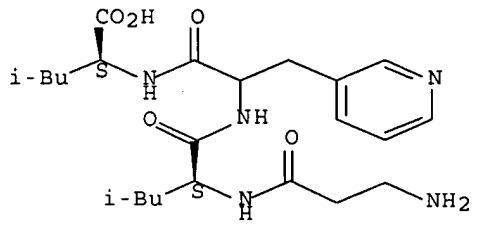
RN 274912-06-0 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



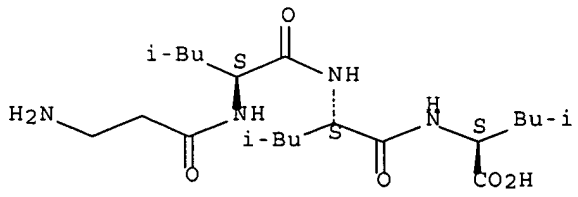
RN 274912-07-1 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-3-(3-pyridinyl)alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



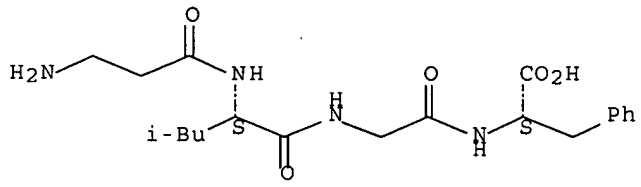
RN 274912-08-2 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



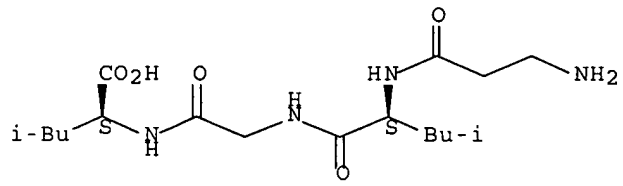
RN 274912-09-3 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-leucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



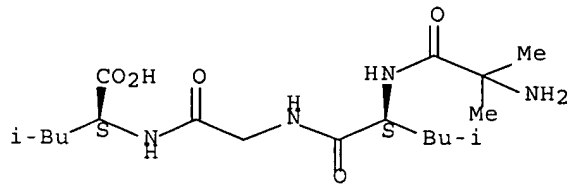
RN 274912-12-8 HCAPLUS
CN L-Leucine, β-alanyl-L-leucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



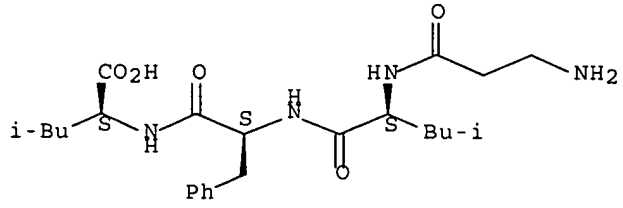
RN 274912-13-9 HCAPLUS
CN L-Leucine, 2-methylalanyl-L-leucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



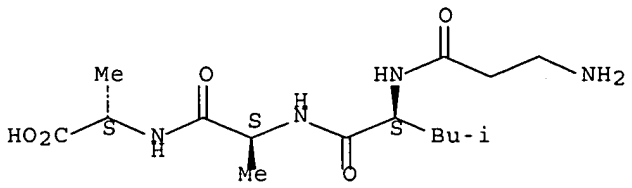
RN 274912-15-1 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



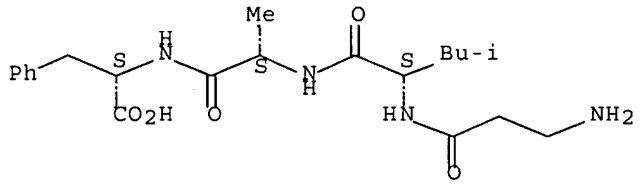
RN 274912-17-3 HCAPLUS
CN L-Alanine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



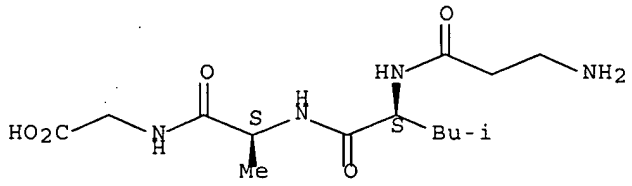
RN 274912-19-5 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



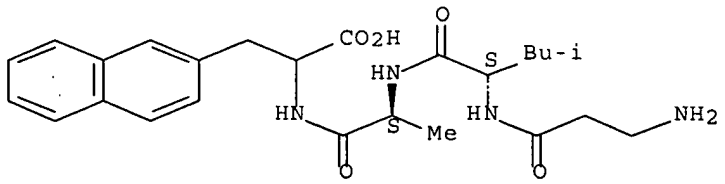
RN 274912-20-8 HCAPLUS
CN Glycine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274912-32-2 HCAPLUS
CN Alanine, β-alanyl-L-leucyl-L-alanyl-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

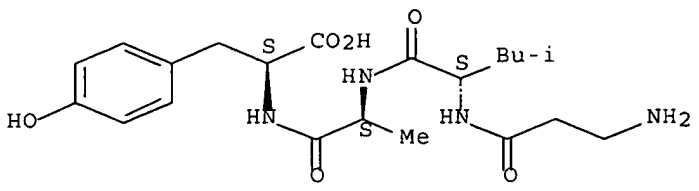
Absolute stereochemistry.



RN 274912-34-4 HCAPLUS

CN L-Tyrosine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

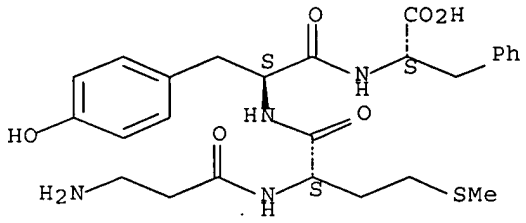
Absolute stereochemistry.



RN 274912-35-5 HCAPLUS

CN L-Phenylalanine, β-alanyl-L-methionyl-L-tyrosyl- (9CI) (CA INDEX NAME)

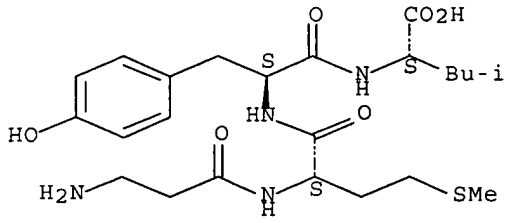
Absolute stereochemistry.



RN 274912-36-6 HCAPLUS

CN L-Leucine, β-alanyl-L-methionyl-L-tyrosyl- (9CI) (CA INDEX NAME)

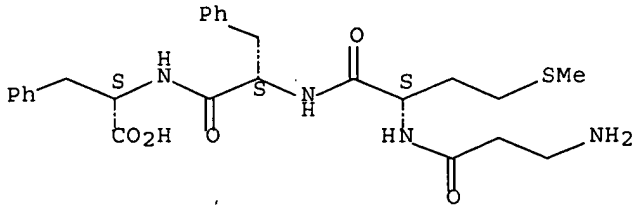
Absolute stereochemistry.



RN 274912-39-9 HCAPLUS

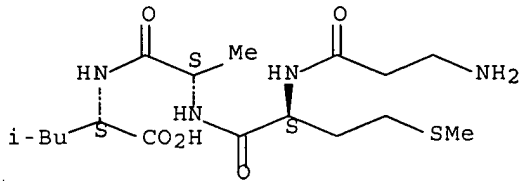
CN L-Phenylalanine, β-alanyl-L-methionyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



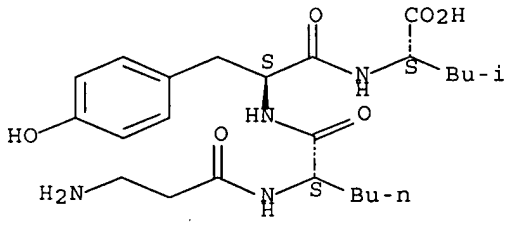
RN 274912-44-6 HCAPLUS
CN L-Leucine, β-alanyl-L-methionyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



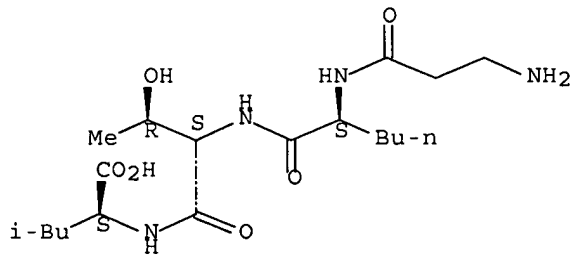
RN 274912-47-9 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274912-49-1 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucyl-L-threonyl- (9CI) (CA INDEX NAME)

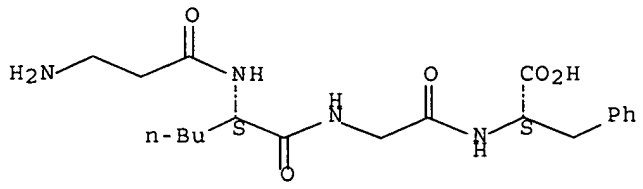
Absolute stereochemistry.



RN 274912-50-4 HCAPLUS

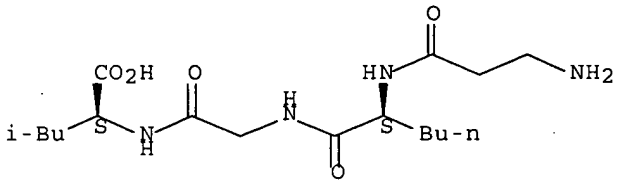
CN L-Phenylalanine, β-alanyl-L-norleucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



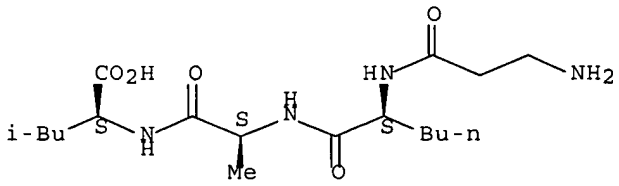
RN 274912-52-6 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



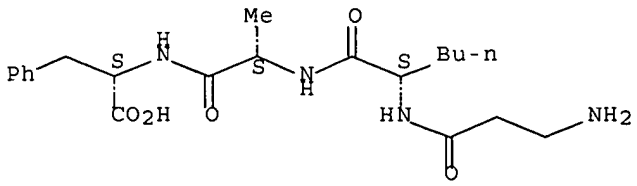
RN 274912-55-9 HCAPLUS
CN L-Leucine, β-alanyl-L-norleucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274912-56-0 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-norleucyl-L-alanyl- (9CI) (CA INDEX NAME)

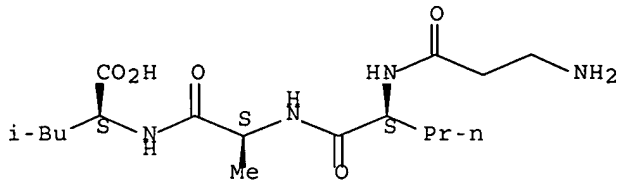
Absolute stereochemistry.



RN 274912-57-1 HCAPLUS

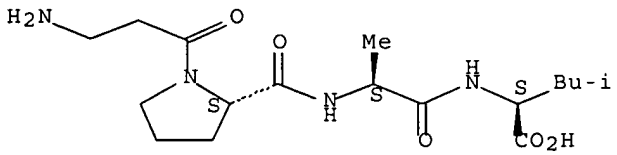
CN L-Leucine, β-alanyl-L-norvalyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



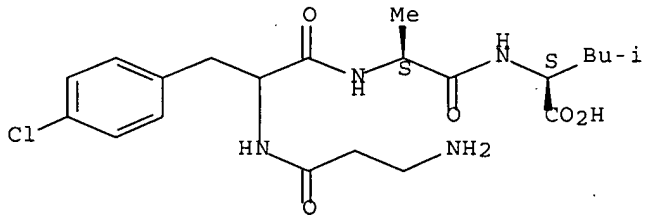
RN 274912-62-8 HCAPLUS
CN L-Leucine, β-alanyl-L-prolyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



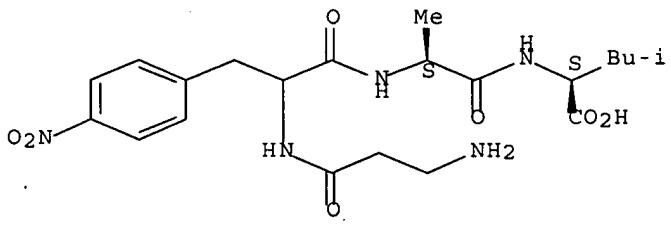
RN 274912-63-9 HCAPLUS
CN L-Leucine, β-alanyl-4-chlorophenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



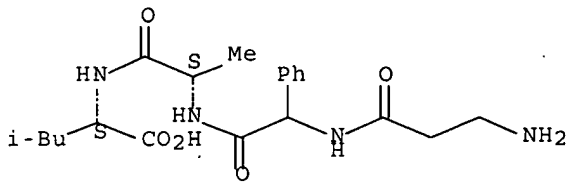
RN 274912-65-1 HCAPLUS
CN L-Leucine, β-alanyl-4-nitrophenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



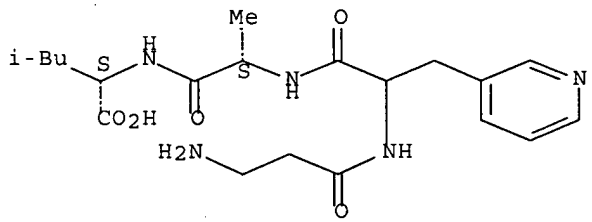
RN 274912-66-2 HCAPLUS
CN L-Leucine, β-alanyl-2-phenylglycyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



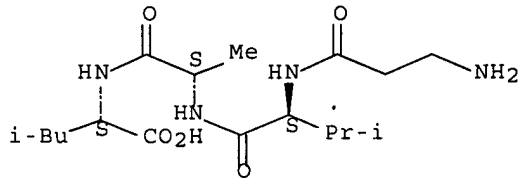
RN 274912-67-3 HCAPLUS
CN L-Leucine, β-alanyl-3-(3-pyridinyl)alanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



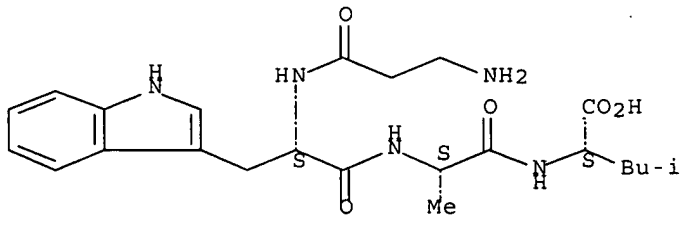
RN 274912-73-1 HCAPLUS
CN L-Leucine, β-alanyl-L-valyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



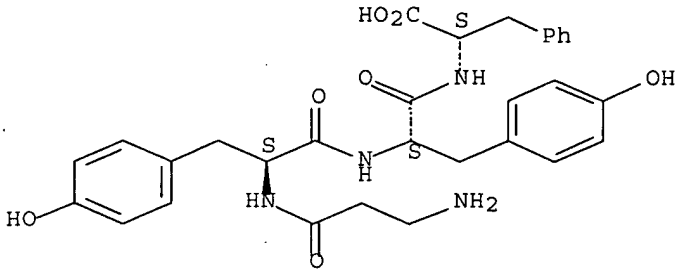
RN 274912-74-2 HCAPLUS
CN L-Leucine, β-alanyl-L-tryptophyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



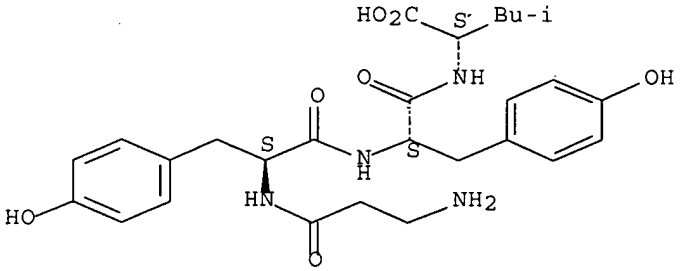
RN 274912-75-3 HCAPLUS
CN L-Phenylalanine, β-alanyl-L-tyrosyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



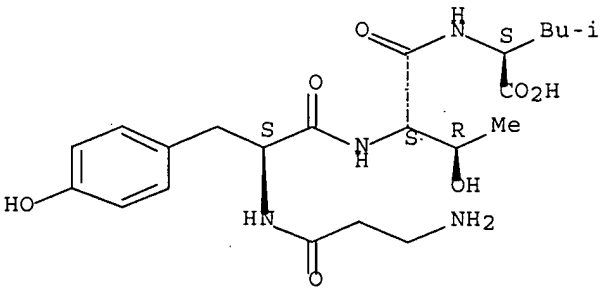
RN 274912-77-5 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



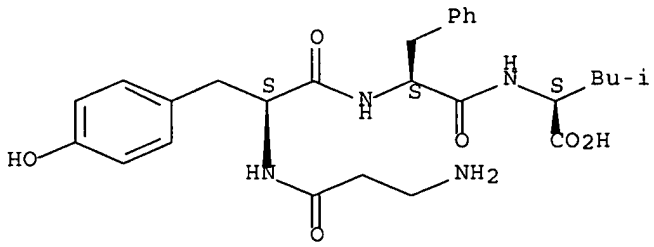
RN 274912-78-6 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



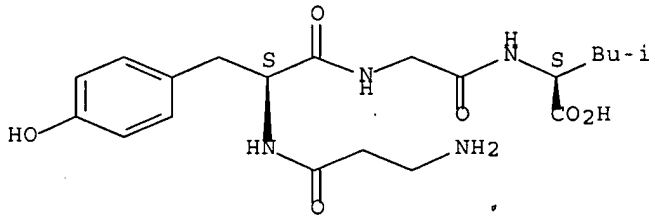
RN 274912-79-7 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



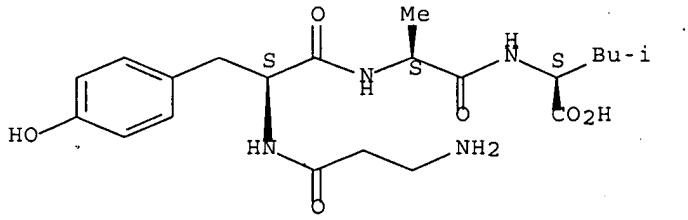
RN 274912-82-2 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274912-86-6 HCAPLUS
CN L-Leucine, β-alanyl-L-tyrosyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

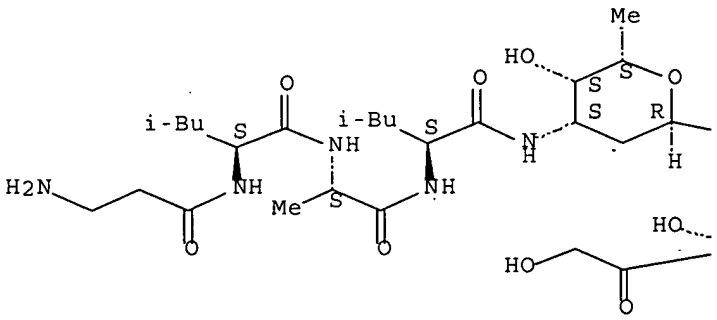


IT **177953-52-5 274912-87-7 274912-88-8**
274912-89-9 274912-90-2 274912-91-3
274912-92-4 274912-93-5 274912-94-6
274912-95-7 274912-96-8 274912-97-9
274912-99-1 274913-02-9 274913-03-0
274913-04-1 274913-05-2 274913-06-3
274913-07-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligopeptide prodrug compds. and process for preparation thereof)
RN 177953-52-5 HCAPLUS
CN 5,12-Naphthacenedione, 10-[[3-[(β-alanyl-L-leucyl-L-alanyl-L-leucyl)amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI)

(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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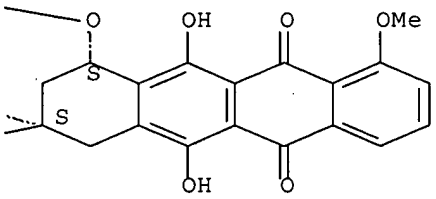
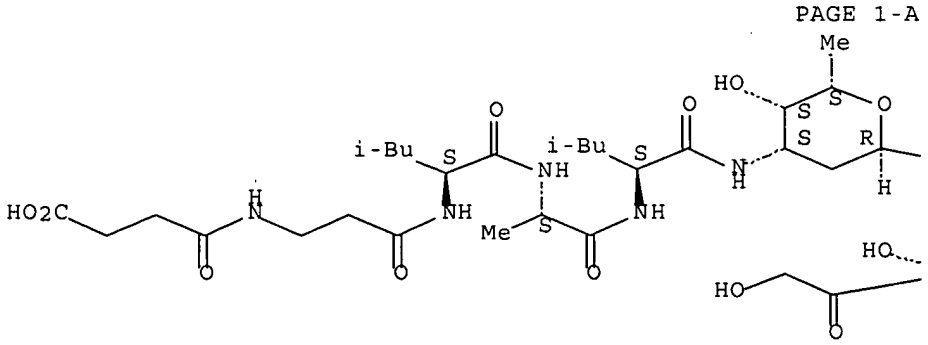


RN 274912-87-7 HCAPLUS

CN 5,12-Naphthacenedione, 10-[[3-[[N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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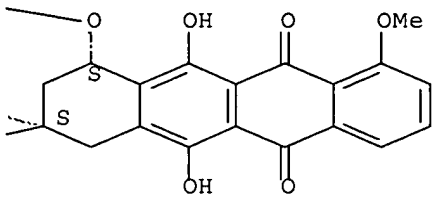
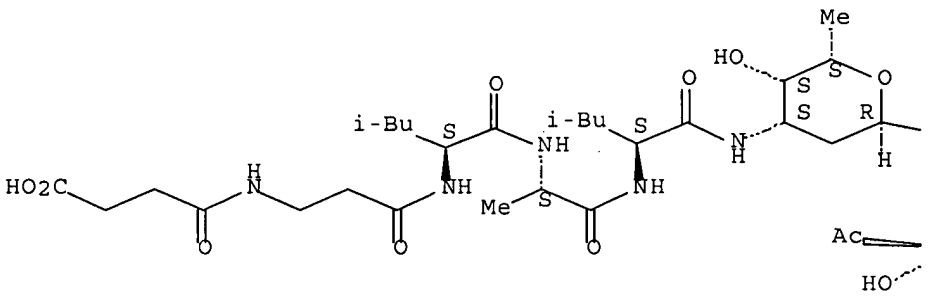


RN 274912-88-8 HCAPLUS

CN 5,12-Naphthacenedione, 8-acetyl-10-[[3-[[N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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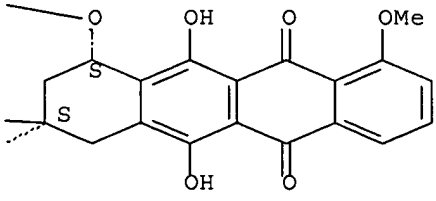
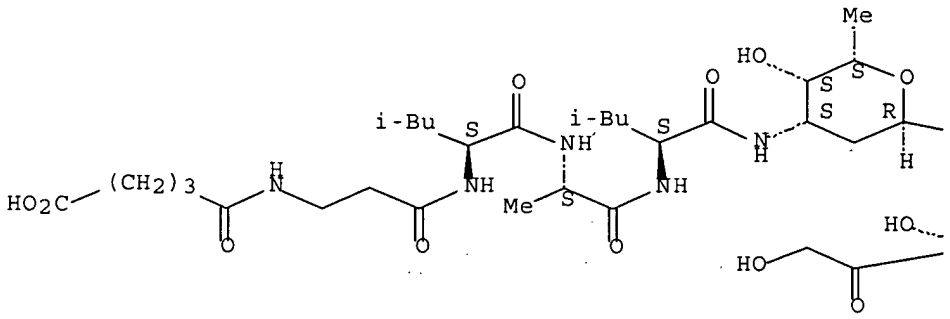


RN 274912-89-9 HCAPLUS

CN 5,12-Naphthacenedione, 10-[[3-[[N-(4-carboxy-1-oxobutyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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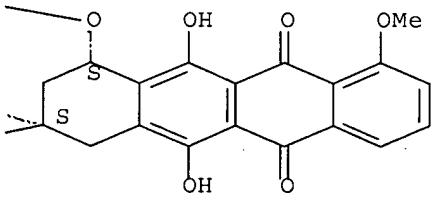
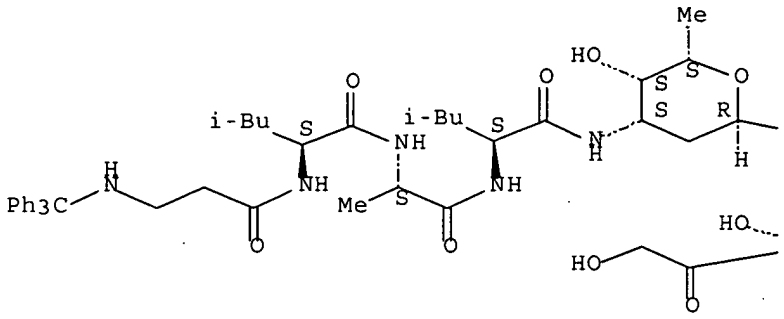


RN 274912-90-2 HCAPLUS

CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-(triphenylmethyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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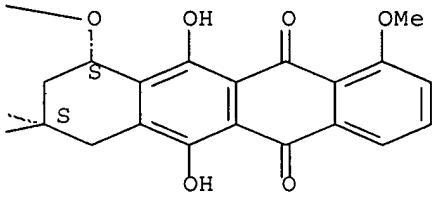
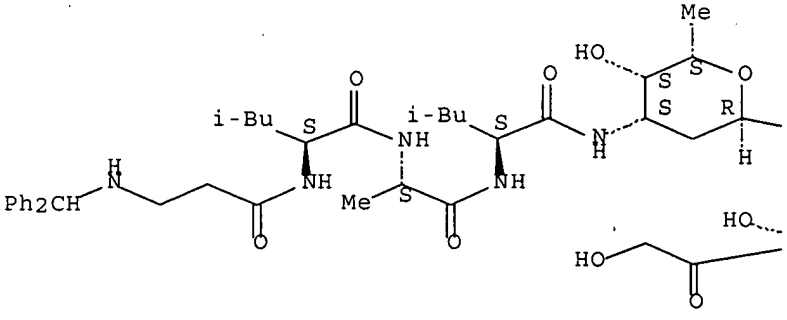


RN 274912-91-3 HCAPLUS

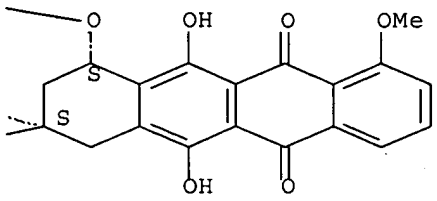
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-(diphenylmethyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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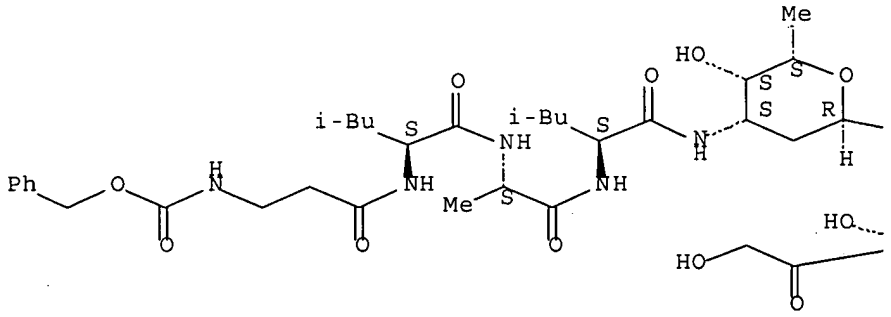
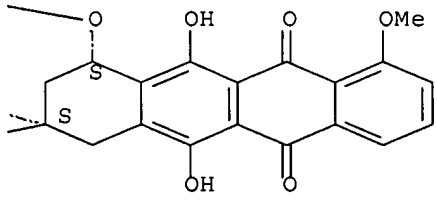
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-[(phenylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

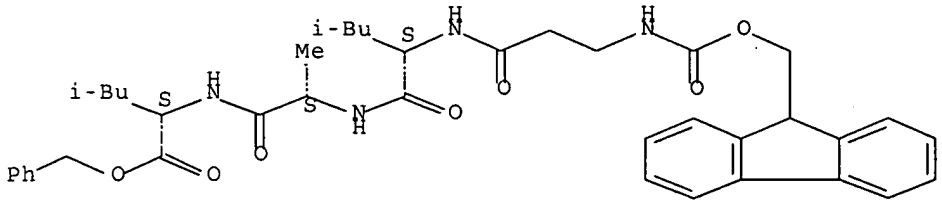


PAGE 1-B



RN 274912-93-5 HCAPLUS
CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

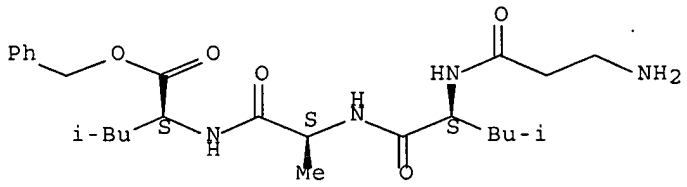
Absolute stereochemistry.



RN 274912-94-6 HCAPLUS

CN L-Leucine, β-alanyl-L-leucyl-L-alanyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

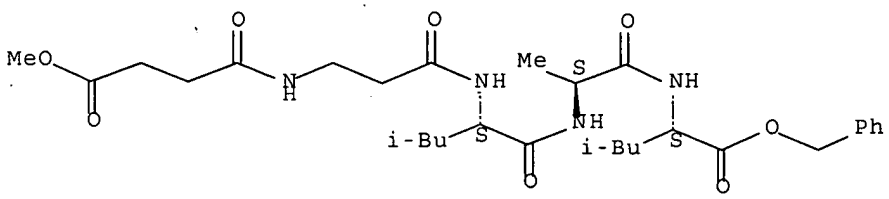
Absolute stereochemistry.



RN 274912-95-7 HCAPLUS

CN L-Leucine, N-(4-methoxy-1,4-dioxobutyl)-β-alanyl-L-leucyl-L-alanyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

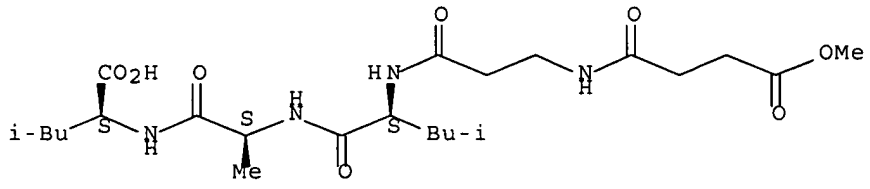
Absolute stereochemistry.



RN 274912-96-8 HCAPLUS

CN L-Leucine, N-(4-methoxy-1,4-dioxobutyl)-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

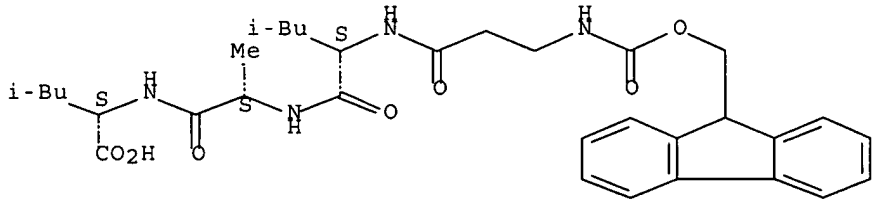
Absolute stereochemistry.



RN 274912-97-9 HCAPLUS

CN L-Leucine, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

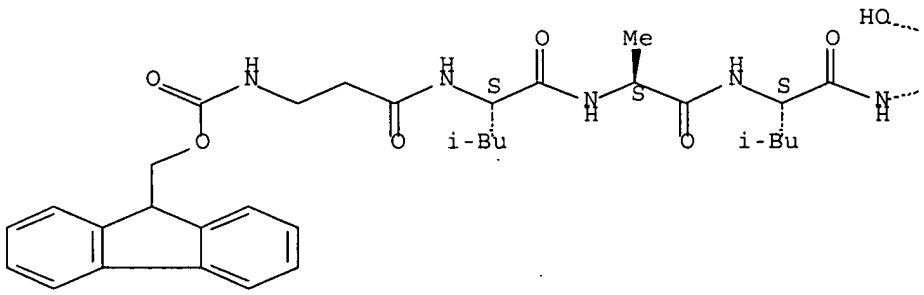


RN 274912-99-1 HCAPLUS

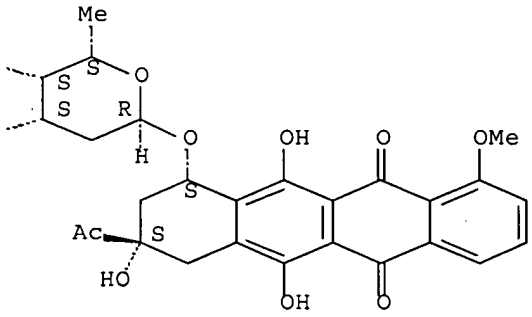
CN 5,12-Naphthacenedione, 8-acetyl-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 274913-02-9 HCAPLUS

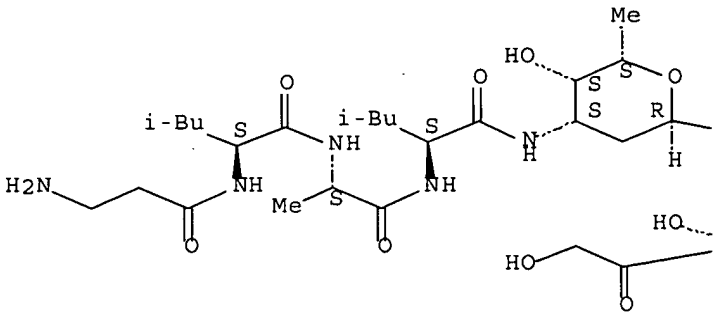
CN Propanoic acid, 2-hydroxy-, compd. with (8S,10S)-10-[[3-[(β-alanyl-L-leucyl-L-alanyl-L-leucyl)amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (1:1) (9CI) (CA INDEX NAME)

CM 1

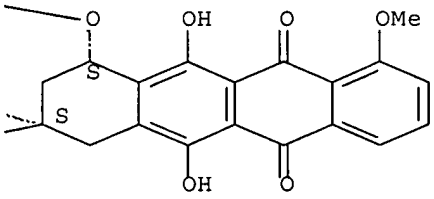
CRN 177953-52-5
CMF C45 H61 N5 O15

Absolute stereochemistry.

PAGE 1-A

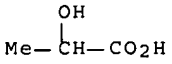


PAGE 1-B



CM 2

CRN 50-21-5
CMF C3 H6 O3

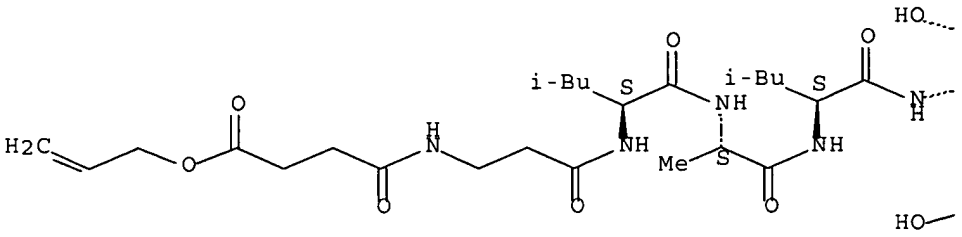


RN 274913-03-0 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-[1,4-dioxo-4-(2-

propenyloxy)butyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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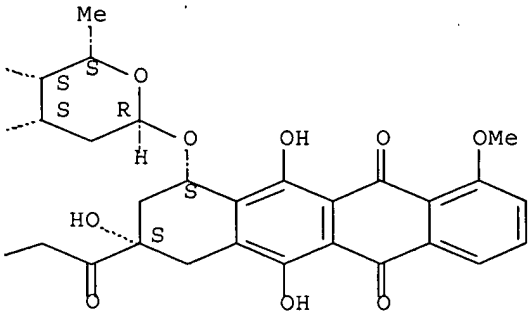
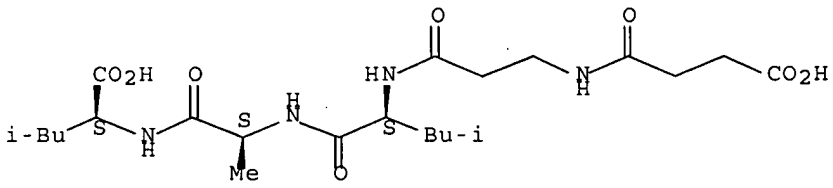


RN 274913-04-1 HCAPLUS

CN L-Leucine, N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

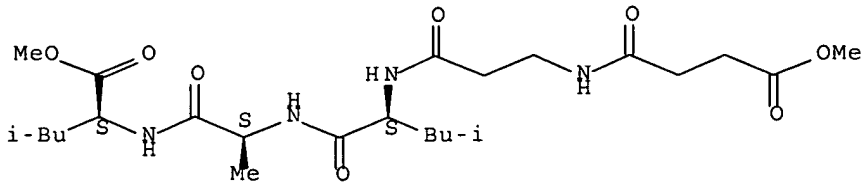
Absolute stereochemistry.



RN 274913-05-2 HCAPLUS

CN L-Leucine, N-(4-methoxy-1,4-dioxobutyl)-β-alanyl-L-leucyl-L-alanyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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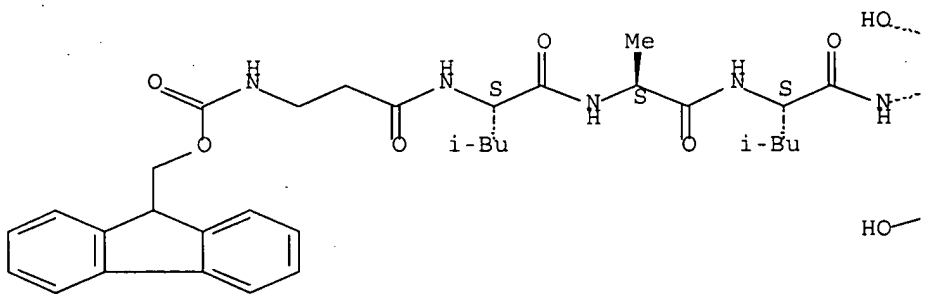
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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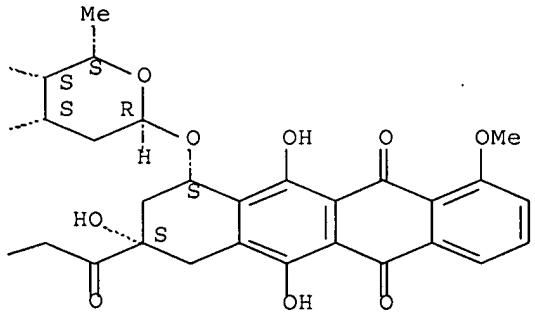
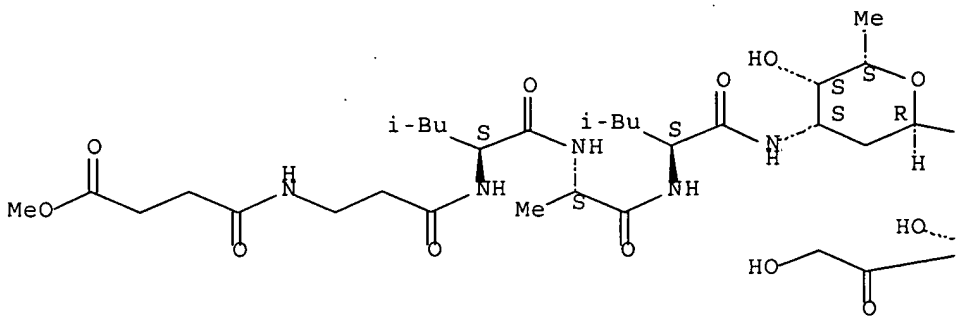


RN 274913-07-4 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-(4-methoxy-1,4-dioxobutyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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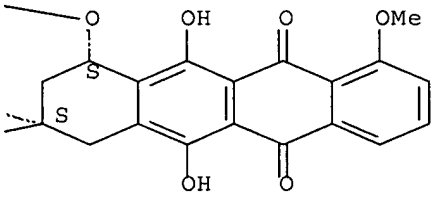


L7 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:98300 HCAPLUS Full-text
DOCUMENT NUMBER: 132:132356
TITLE: Chemically induced intracellular hyperthermia for **therapeutic** and diagnostic use
INVENTOR(S): Bachynsky, Nicholas; Roy, Woodie
PATENT ASSIGNEE(S): Texas Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006143	A1	20000210	WO 1999-US16940	19990727

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2337690	AA	20000210	CA 1999-2337690	19990727
AU 9951318	A1	20000221	AU 1999-51318	19990727
AU 750313	B2	20020718		
EP 1098641	A1	20010516	EP 1999-935949	19990727

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:	US 1998-94286P	P	19980727
	WO 1999-US16940	W	19990727

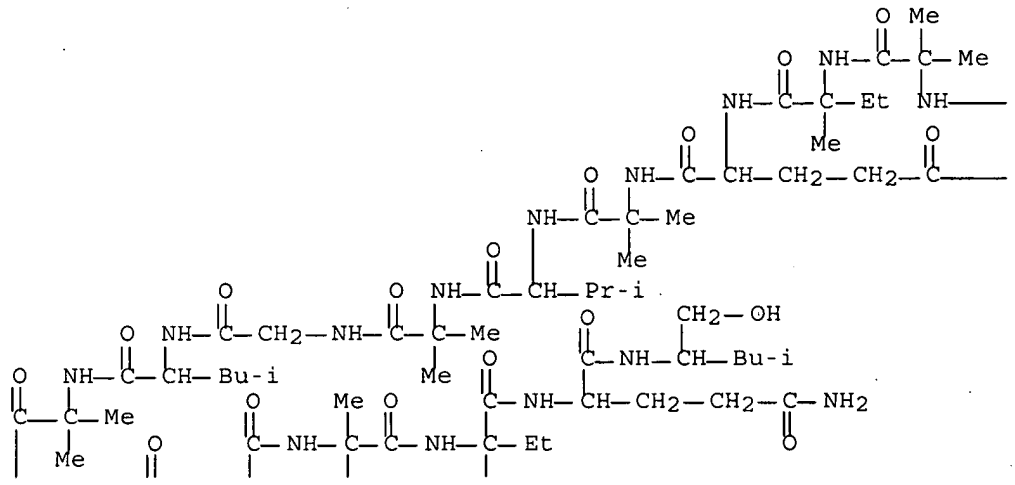
AB **Therapeutic** pharmacol. agents and methods are disclosed for chemical induction of intracellular hyperthermia and/or free radicals for the diagnosis and treatment of infections, malignancy, and other medical conditions. A process and composition are provided for the diagnosis or killing of cancer cells and inactivation of susceptible bacterial, parasitic, fungal, and viral pathogens by chemical generating heat, and/or free radicals and/or hyperthermia-inducible immunogenic determinants by using mitochondrial uncoupling agents, especially 2,4-dinitrophenol, and their **conjugates**, either alone or in combination with other drugs, hormones, cytokines and radiation.

IT **171980-70-4**, Trichorzin HA V
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical induced intracellular hyperthermia for diagnostic and **therapeutic** use, and use with other agents)

RN 171980-70-4 HCAPLUS

CN Trichorzin HA V (9CI) (CA INDEX NAME)

PAGE 1-A



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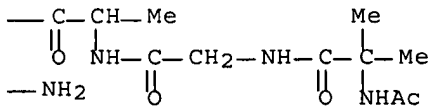
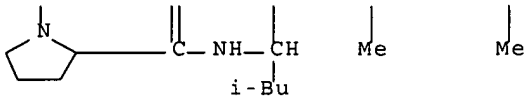




REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:165250 HCAPLUS Full-text
DOCUMENT NUMBER: 126:154826
TITLE: Functional surrogates of analytes of interest and methods of obtaining and using same
INVENTOR(S): Lee-Own, F. Victor; Carter, John Mark
PATENT ASSIGNEE(S): Cytogen Corporation, USA
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9641172	A1	19961219	WO 1996-US10498	19960607
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9662826	A1	19961230	AU 1996-62826	19960607
PRIORITY APPLN. INFO.:			US 1995-476375 A	19950607
			WO 1996-US10498 W	19960607

AB Functional surrogates are disclosed which serve as mimics of naturally occurring mols., such as analytes of interest present in a given sample. In particular, functional surrogates (including epitopes and mimetopes) of macromol. moieties, including large to medium-sized proteins, are described. The functional surrogates of the present invention are useful in a variety of diagnostic, prophylactic, and **therapeutic** applications. Indeed, where the detection of a macromol. moiety is hampered by its size, a functional surrogate of the present invention, serving as the mimic of the macromol. moiety, may be better suited for a given diagnostic assay. Methods of obtaining functional surrogates, various methods of their use, and compns., including kits, are also described. Accordingly, certain binding peptides, including those of a well-defined sequence, have been discovered, which can be used in a number of affinity assays, including those utilizing fluorescence polarization immunoassay (FPIA), enzyme multiplied immunoassay technique (EMIT), or cloned enzyme donor immunoassays (CEDIA), to name a few.

IT **186743-67-9P**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

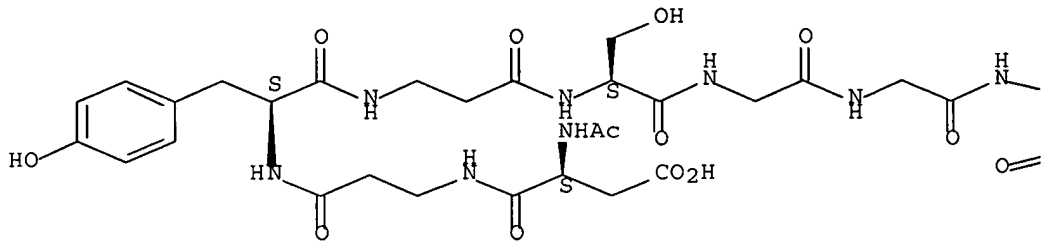
(functional surrogates of analytes for affinity assays including immunoassays)

RN 186743-67-9 HCAPLUS

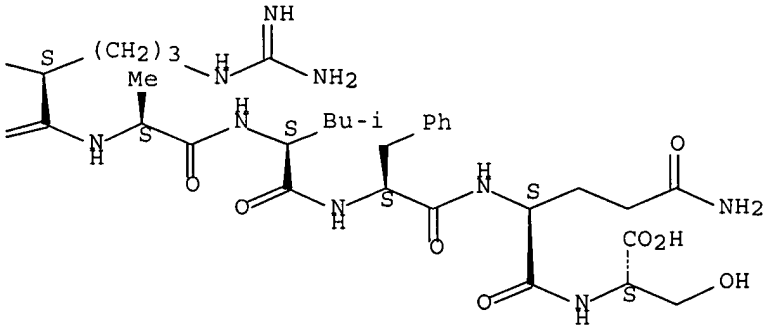
CN L-Serine, N-acetyl-L-α-aspartyl-β-alanyl-L-tyrosyl-β-alanyl-L-serylglycylglycyl-L-arginyl-L-alanyl-L-leucyl-L-phenylalanyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L7 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:377089 HCAPLUS Full-text

DOCUMENT NUMBER: 125:49345

TITLE: Compounds, pharmaceutical composition and diagnostic system comprising same, and their use

INVENTOR(S): Trouet, Andre; Baurain, Roger

PATENT ASSIGNEE(S): La Region Wallonne, Belg.; Baurain, Roger

SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9605863	A1	19960229	WO 1995-BE76	19950821

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RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

BE 1008580	A3	19960604	BE 1994-751	19940819
BE 1008581	A3	19960604	BE 1994-752	19940819
CA 2203622	AA	19960229	CA 1995-2203622	19950821
AU 9532486	A1	19960314	AU 1995-32486	19950821
AU 694546	B2	19980723		
EP 769967	A1	19970502	EP 1995-928905	19950821
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508291	T2	19980818	JP 1995-507662	19950821
NO 9700748	A	19970410	NO 1997-748	19970218
US 5962216	A	19991005	US 1997-793910	19970401
US 6342480	B1	20020129	US 1999-298330	19990423
US 2002160943	A1	20021031	US 2001-12576	20011109

PRIORITY APPLN. INFO.:	BE 1994-751	A	19940819
	BE 1994-752	A	19940819
	WO 1995-BE76	W	19950821
	US 1997-793910	A1	19970401
	US 1999-298330	A1	19990423

OTHER SOURCE(S): MARPAT 125:49345

AB The compds. W-Z-M of the invention comprise an element M, selected from markers and **therapeutic** agents having an intracellularly active site, linked to a ligand W-Z having an arm Z linked to a terminal group W. The bond between the arm Z of the ligand W-Z and the element M prevents the compound (W-Z-M) from penetrating within the cells and/or inhibits expression of the marker M. This bond is selectively cleaved by factors secreted by target cells so as to enable the marker M to be expressed in the target cells or the **therapeutic** agent M to penetrate therein; the terminal group W ensures that the compound (W-Z-M) is stable in serum and circulating blood. Data are presented for e.g. effect of β-Ala-L-Leu-L-Ala-L-Leu-daunorubicin **conjugate** with mammary carcinoma cells. Also described is characterization of protease(s) secreted into the extracellular medium and able to hydrolyze β-Ala-Leu-Ala-Leu-doxorubicin.

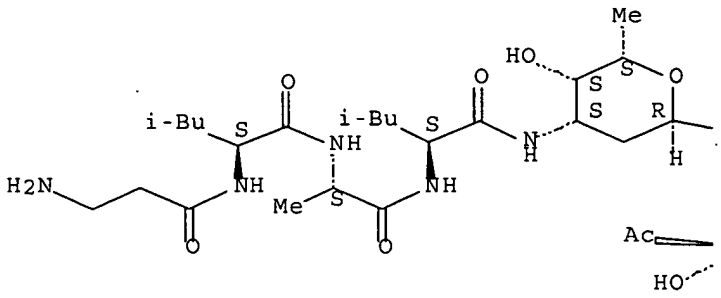
IT **177953-51-4P 177953-52-5P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(drug **conjugates** and marker **conjugates** with cleavable bond, pharmaceutical compns., and diagnostic system)

RN 177953-51-4 HCAPLUS

CN 5,12-Naphthacenedione, 8-acetyl-10-[[3-[[N-[N-[N-(3-amino-1-oxopropyl)-L-leucyl]-L-alanyl]-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-, (8S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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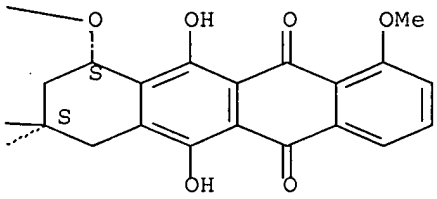
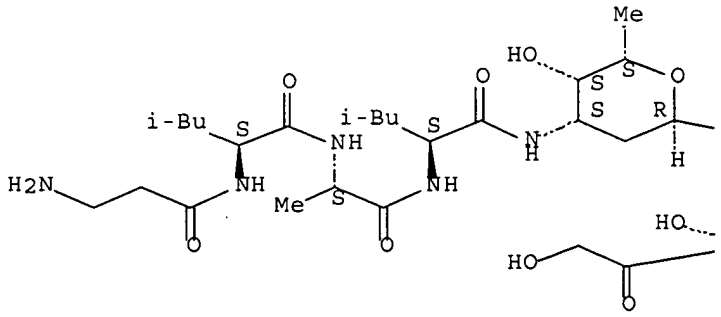


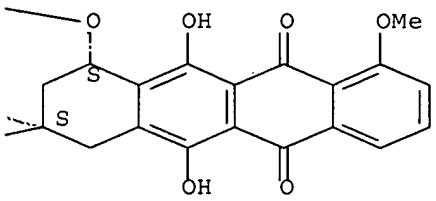
RN 177953-52-5 HCAPLUS

CN 5,12-Naphthacenedione, 10-[[3-[(β-alanyl-L-leucyl-L-alanyl-L-leucyl)amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

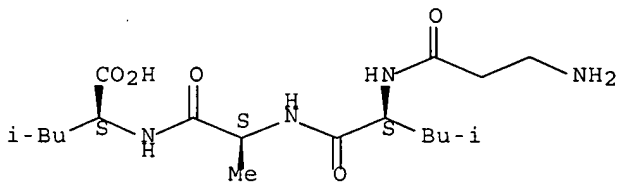
PAGE 1-A





IT 177953-71-8D, reaction products with coumarin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(drug **conjugates** and marker **conjugates** with cleavable bond, pharmaceutical compns., and diagnostic system)
RN 177953-71-8 HCAPLUS
CN L-Leucine, β-alanyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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 NEWS  3  FEB 28  PATDPAFULL - New display fields provide for legal status
                  data from INPADOC
 NEWS  4  FEB 28  BABS - Current-awareness alerts (SDIs) available
 NEWS  5  MAR 02  GBFULL: New full-text patent database on STN
 NEWS  6  MAR 03  REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  7  MAR 03  MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 22  KOREAPAT now updated monthly; patent information enhanced
 NEWS  9  MAR 22  Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  10 MAR 22  PATDPASPC - New patent database available
 NEWS  11 MAR 22  REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS  12 APR 04  EPFULL enhanced with additional patent information and new
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 NEWS  13 APR 04  EMBASE - Database reloaded and enhanced
 NEWS  14 APR 18  New CAS Information Use Policies available online
 NEWS  15 APR 25  Patent searching, including current-awareness alerts (SDIs),
                  based on application date in CA/CAplus and USPATFULL/USPAT2
                  may be affected by a change in filing date for U.S.
                  applications.
 NEWS  16 APR 28  Improved searching of U.S. Patent Classifications for
                  U.S. patent records in CA/CAplus
 NEWS  17 MAY 23  GBFULL enhanced with patent drawing images
 NEWS  18 MAY 23  REGISTRY has been enhanced with source information from
                  CHEMCATS
 NEWS  19 JUN 06  STN Patent Forums to be held in June 2005
 NEWS  20 JUN 06  The Analysis Edition of STN Express with Discover!
                  (Version 8.0 for Windows) now available
 NEWS  21 JUN 13  RUSSIAPAT: New full-text patent database on STN
 NEWS  22 JUN 13  FRFULL enhanced with patent drawing images
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 NEWS  23 JUN 20  MEDICONF to be removed from STN

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               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS,
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2005

77 FILES IN THE FILE LIST IN STNINDEX

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search error messages that display as 0* with SET DETAIL OFF.

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          1   FILE ADISINSIGHT
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          3   FILE MEDLINE
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          2   FILE USPATFULL
          1   FILE PHAR
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         1   FILE WPIDS
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  21 FILES HAVE ONE OR MORE ANSWERS,   77 FILES SEARCHED IN STNINDEX

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F1           8   TOXCENTER
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L3   ANSWER 1 OF 24 USPATFULL on STN   DUPLICATE 1
ACCESSION NUMBER: 2005:30747 USPATFULL Full-text
TITLE: Allosteric probes and methods
INVENTOR(S):   Nilsen-Hamilton, Marit, Ames, IA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005026178	A1	20050203
APPLICATION INFO.:	US 2004-809886	A1	20040326 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-457936P	20030328 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DICKSTEIN SHAPIRO MORIN & OSHINSKY LLP, 2101 L Street, NW, Washington, DC, 20037
NUMBER OF CLAIMS: 55
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 1198
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . fluids from these cancers. PSA has been targeted with peptide-based prodrugs linked with toxic agents, doxorubicin or thapsigargen. The prodrugs **CPI-0004Na** and L-377202 comprise peptides linked to doxorubicin.
CLM What is claimed is:
11. The probe of claim 9, wherein the prodrug is selected from the group consisting of **CPI-0004Na** and L-377202.

13. The probe of claim 10, where the prodrug is selected from the group consisting of **CPI-0004Na** and L-377202.

34. The method of claim 32, wherein the prodrug is selected from the group consisting of **CPI-0004Na** and L-377202.

37. The method of claim 33, wherein the prodrug is selected from the group consisting of **CPI-0004Na** and L-377202.

52. The method of claim 50, wherein the prodrug is selected from the group consisting of **CPI-0004Na** and L-377202.

L3 ANSWER 2 OF 24 USPATFULL on STN
ACCESSION NUMBER: 2005:81108 USPATFULL Full-text
TITLE: Targeted ligands
INVENTOR(S): Herman, William, Thornhill, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005069549	A1	20050331
APPLICATION INFO.:	US 2004-501453	A1	20041122 (10)
	WO 2003-CA44		20030114

	NUMBER	DATE
PRIORITY INFORMATION:	CA 2002-2368708	20020114
	WO 2002-CA317	20020311
	CA 2002-2397169	20020813
	CA 2002-2402930	20020919

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BERESKIN AND PARR, SCOTIA PLAZA, 40 KING STREET WEST-SUITE 4000 BOX 401, TORONTO, ON, M5H 3Y2
NUMBER OF CLAIMS: 21

EXEMPLARY CLAIM: 1
LINE COUNT: 9273
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . US patent application 20020103133, WO02/060488, WO02/072620, WO 96105863, U.S. Pat. No. 5,962,216, WO01/95943, WO02/00263, WO01/68145, WO01/36003, Dubois V, et al. **CPI-0004Na**, a new extracellularly tumor-activated prodrug of doxorubicin: invivo toxicity, activity, and tissue distribution confirm tumor cell selectivity. Cancer Res. 2002. . .

L3 ANSWER 3 OF 24 TOXCENTER COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:234181 TOXCENTER Full-text
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA14120325667W
TITLE: Allosteric nucleic acid probes and their use in disease diagnosis and treatment
AUTHOR(S): Nilsen-Hamilton, Marit
CORPORATE SOURCE: ASSIGNEE: Iowa State University Research Foundation, Inc.
PATENT INFORMATION: WO 2004088279 A2 14 Oct 2004
SOURCE: (2004) PCT Int. Appl., 47 pp.
CODEN: PIXXD2.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2004:857758
LANGUAGE: English
ENTRY DATE: Entered STN: 20041019
Last Updated on STN: 20050104
RN 32986-56-4 (Tobramycin)
13981-56-1 (Fluorine-18)
14133-76-7 (Technetium-99)
207395-85-5 (L-377202)
274912-87-7 (**CPI-0004Na**)
57-92-1 (Streptomycin)
1404-04-2 (Neomycin)
26787-78-0 (Amoxicillin)
56-65-5 (ATP)
58-55-9 (Theophylline)
61-19-8 (AMP)
74-79-3 (Arginine)
119-04-0 (Neomycin B)
146-17-8 (FMN)
372-75-8. . .

L3 ANSWER 4 OF 24 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004242318 EMBASE Full-text
TITLE: Anthracyclines: Molecular advances and pharmacologie developments in antitumor activity and cardiotoxicity.
AUTHOR: Minotti G.; Menna P.; Salvatorelli E.; Cairo G.; Gianni L.
CORPORATE SOURCE: Dr. G. Minotti, G. d'Annunzio Univ. Sch. of Medicine, Centro Studi sull'Invecchiamento, Via dei Vestini, 66013 Chieti, Italy. gminotti@unich.it
SOURCE: Pharmacological Reviews, (2004) Vol. 56, No. 2, pp. 185-229.
Refs: 375
ISSN: 0031-6997 CODEN: PAREAQ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer

037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040715
Last Updated on STN: 20040715
CT Medical Descriptors:
*cancer: . . .
trial
*doxorubicin: AN, drug analysis
*doxorubicin: CB, drug combination
*doxorubicin: CM, drug comparison
*doxorubicin: DO, drug dose
*doxorubicin: IT, drug interaction
*doxorubicin: DT, drug therapy
*doxorubicin: PK, pharmacokinetics
***doxorubicin: PD, pharmacology**
*daunorubicin: AE, adverse drug reaction
*daunorubicin: CT, clinical trial
*daunorubicin: AN, drug analysis
*daunorubicin: CR, drug concentration
*daunorubicin: DO, drug dose
*daunorubicin: DT, drug. . .
1 yl]benzenesulfonamide: DV, drug development
antioxidant
iron chelate: AN, drug analysis
razoxane: AN, drug analysis
unindexed drug
unclassified drug
1,2 propanediamine n,n' diacetamide n,n' diacetic acid
evacet
l 377202
cpi 0004na
pk 2
3' deamino 3' morpholinooxaunomycin
mx 2
nemorubicin
pnu 159548
4 demethoxy 14 hydroxydaunomycinone 7 o [4 o (3 amino 2,3,6 trideoxy alpha lyxo. . .
CN. . . Ad 288; Ad 32; Ad 198; Men 10755; Pnu 159548; Pnu 152243; Fce 23762; Mx 2; Krn 8602; Pk 2; **Cpi 0004na**; L 377202; Tlc d 99; Daunoxome; Myocet; Evacet; Caelyx; Doxil; Adr 925; Adr 529; Icrf 187; Bms 184476; Sc. . .

L3 ANSWER 5 OF 24 TOXCENTER COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:210428 TOXCENTER Full-text
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA14207106748R
TITLE: **CPI-0004Na**, a new doxorubicin prodrug, reduces growth of 3LL-H61 carcinoma lung metastases in C57B1/6 mice
AUTHOR(S): Dasnols, Luc; Lebtahi, Karim; Abarca-Quinones, Jorge; Havaux, Nathalie; Dupont, Samuel; Dubois, Vincent; Trouet, Andre
CORPORATE SOURCE: Laboratory of Cell Biology & Institut des Sciences de la Vie, Universite catholique de Louvain, Louvain-La-Neuve, B-1348, Belg..
SOURCE: Journal of Experimental Therapeutics and Oncology, (2004) Vol. 4, No. 2, pp. 167-169.

CODEN: JETOFX. ISSN: 1359-4117.
COUNTRY: BELGIUM
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2004:765541
LANGUAGE: English
ENTRY DATE: Entered STN: 20040921
Last Updated on STN: 20050308

TI **CPI-0004Na**, a new doxorubicin prodrug, reduces growth of 3LL-H61 carcinoma lung metastases in C57B1/6 mice

AB. . . approach developed to overcome the lack of selectivity and the side effects responsible for the limited efficacy of chemotherapeutic agents. **CPI-0004Na**, a doxorubicin (Dox) prototype prodrug of this type, is less toxic than free Dox and showed increased efficacy against s.c.. . . carcinoma lung metastases in mice. Our results indicate that, Dox has no effect on the number of lung metastases while **CPI-0004Na** induces a 38.3% reduction on average When considering the effect on the proportion of the lungs' surface covered by metastases, Dox induces a 39% reduction while the prodrug **CPI-0004Na** is about two fold more active with a 71% decrease.

RN 23214-92-8 (Doxorubicin)
274912-87-7 (**CPI 0004Na**)

L3 ANSWER 6 OF 24 PROMT COPYRIGHT 2005 Gale Group on STN

ACCESSION NUMBER: 2003:127876 PROMT Full-text
TITLE: Anticancer Agents From Antibiotic Sources - New Antibiotics, Analogs and Derivatives, and Targeted Cytotoxics - a Report From New Medicine.
SOURCE: PR Newswire, (29 Apr 2003) pp. LATU12529042003.
PUBLISHER: PR Newswire Association, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 708
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

TX Among novel prodrugs are CPI-0004 (**CPI-0004Na**), CRX-103, L-377202, etc. Novel formulations include liposome-encapsulated doxorubicin (LED), MTC-DOX, P80DOX-NP, Resmycin, SMANCS, SYN 2002, and Transdrug Doxorubicin.

L3 ANSWER 7 OF 24 TOXCENTER COPYRIGHT 2005 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2003:232545 TOXCENTER Full-text
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA14011156884M
TITLE: CD10 Is a Key Enzyme Involved in the Activation of Tumor-activated Peptide Prodrug **CPI-0004Na** and Novel Analogues: Implications for the Design of Novel Peptide Prodrugs for the Therapy of CD10+ Tumors
AUTHOR(S): Pan, Chin; Cardarelli, Pina M.; Nieder, Matthew H.; Pickford, Lesley B.; Gangwar, Sanjeev; King, David J.; Yarranton, Geoffrey T.; Buckman, Dana; Roscoe, William; et al.
CORPORATE SOURCE: Corixa Corp., South San Francisco, CA, 94080, USA.
SOURCE: Cancer Research, (2003) Vol. 63, No. 17, pp. 5526-5531.
CODEN: CNREA8. ISSN: 0008-5472.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2003:733803

LANGUAGE: English
ENTRY DATE: Entered STN: 20030923
Last Updated on STN: 20040309

TI CD10 Is a Key Enzyme Involved in the Activation of Tumor-activated Peptide Prodrug **CPI-0004Na** and Novel Analogues: Implications for the Design of Novel Peptide Prodrugs for the Therapy of CD10+ Tumors

AB . . . the tumor environment have been explored to improve the therapeutic index of cytotoxic drugs. One such prodrug of doxorubicin (Dox), **CPI-0004Na** [N-succinyl-β-alanyl-L-leucyl-L-alanyl-L-leucyl-Dox (**sALAL-Dox**)] has been shown to have an improved antitumor efficacy profile with reduced toxicity compared with Dox in tumor xenograft models. . . . we demonstrate that CD10, a cell surface metalloprotease expressed on a variety of tumor cell types, is capable of cleaving **CPI-0004Na** and related peptide prodrugs such as N-succinyl-β-alanyl-L-isoleucyl-L-alanyl-L-leucyl-Dox (sAIAL-Dox). This proteolytic cleavage generates leucyl-Dox, which is capable of entering cells and generating intracellular Dox. In a [3H]thymidine proliferation assay, analogs of **CPI-0004Na** showed a 100-300-fold increase in potency on CD10+ cells compared with CD10- cells. Cytotoxicity of **CPI-0004Na** was inhibited by phosphoramidon, a known inhibitor of CD10 enzymic activity. Furthermore, Chinese hamster ovary CHO-S cells, which are resistant to **CPI-0004Na**, could be sensitized to the cytotoxic effect of the prodrug by transfection of a CD10 cDNA. Tumor xenograft studies using. . . prostate tumor cells support the important role of CD10 in the antitumor efficacy of these prodrugs against tumors expressing CD10. **CPI-0004Na** and sAIAL-Dox achieved statistically significant 70% tumor growth inhibition at day 22. CD10 is expressed on many types of human. . .

ST Miscellaneous Descriptors
metalloprotease CD10 tumor peptide prodrug **CPI 0004Na**

RN 81669-70-7 (Metalloprotease)
23214-92-8 (Doxorubicin)
274912-87-7 (**CPI 0004Na**)
380861-69-8 (SAIAL-Dox)
385449-27-4 (SLAG-Dox)
RN 70774-25-3

L3 ANSWER 8 OF 24 TOXCENTER COPYRIGHT 2005 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2002:105095 TOXCENTER Full-text
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA13717241802R
TITLE: **CPI-0004Na**, a new extracellularly tumor-activated prodrug of Doxorubicin: in vivo toxicity, activity, and tissue distribution confirm tumor cell selectivity
AUTHOR(S): Dubois, Vincent; Dasnois, Luc; Lebtahi, Karim; Collot, Francoise; Heylen, Nathalie; Havaux, Nathalie; Fernandez, Anne-Marie; Lobl, Thomas J.; Oliyai, Cecilia; et al.
CORPORATE SOURCE: Universite Catholique de Louvain, Laboratory of Cell Biology, Louvain-la-Neuve, B-1348, Belg..
SOURCE: Cancer Research, (2002) Vol. 62, No. 8, pp. 2327-2331. CODEN: CNREA8. ISSN: 0008-5472.
COUNTRY: BELGIUM
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2002:323079
LANGUAGE: English
ENTRY DATE: Entered STN: 20020509
Last Updated on STN: 20030624

TI **CPI-0004Na**, a new extracellularly tumor-activated prodrug of Doxorubicin: in vivo toxicity, activity, and tissue distribution confirm tumor cell selectivity

AB. . . normal sensitive cells has been very active for at least 20 yr. The extracellularly tumor-activated peptidic prodrug of doxorubicin (Dox) **CPI-0004Na** (N-succinyl-β-alanyl-L-leucyl-L-alanyl-L-leucyl-Dox) is potentially such a treatment. Here, we report the results of lethality studies performed with this compound in the. . . data indicate that this reduced toxicity is attributable to a lower uptake of Dox in normal tissues after treatment with **CPI-0004Na** than after the administration of an equimolar dose of Dox·HCl. For example, heart exposure to Dox is reduced > 10-fold. Because of this reduced toxicity, higher doses of **CPI-0004Na** than of the parent drug could be used to treat nude mice bearing s.c. human breast (MCF-7/6) and colon (LS-174-T. . . as compared with Dox·HCl. Particularly, LS-174-T tumors that do not respond to Dox were inhibited by 68% after treatment with **CPI-0004Na**. Tissue distribution studies performed with MCF-7/6 tumor-bearing nude mice and comparing **CPI-0004Na** and Dox·HCl confirmed that the improved activity of the prodrug is actually the result of selective generation and uptake of Dox at the tumor site. Dox levels in tumor tissue were 2-fold higher after treatment with **CPI-0004Na** than after treatment with an equimolar dose of Dox·HCl, whereas normal tissue levels were reduced 1.4-29-fold.

L3 ANSWER 9 OF 24 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 6

ACCESSION NUMBER: 2002:554867 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200554867
TITLE: Improved activity of **CPI-0004Na**, a new doxorubicin prodrug, in an experimental metastasis model.
AUTHOR(S): Dasnois, L. [Reprint author]; Lebtahi, K. [Reprint author]; Abarca-Quinones, J. [Reprint author]; Havaux, N. [Reprint author]; Dubois, V. [Reprint author]; Trouet, A. [Reprint author]
CORPORATE SOURCE: Laboratory of Cell Biology, Univerte Catholique de Louvain, Louvain-La-Neuve, Belgium
dasnois@bani.ucl.ac.be
SOURCE: International Journal of Cancer Supplement, (2002) No. 13, pp. 435-436. print.
Meeting Info.: 18th UICC International Cancer Congress. Oslo, Norway. June 30-July 05, 2002.
ISSN: 0898-6924.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Oct 2002
Last Updated on STN: 30 Oct 2002

TI Improved activity of **CPI-0004Na**, a new doxorubicin prodrug, in an experimental metastasis model.

IT . . .
respiratory system
IT Diseases
lung metastasis: neoplastic disease, respiratory system disease
Lung Neoplasms (MeSH); Neoplasm Metastasis (MeSH)
IT Chemicals & Biochemicals
CPI-0004Na: antineoplastic, efficacy, pharmacokinetics, prodrug; doxorubicin: antineoplastic-drug, pharmacokinetics

L3 ANSWER 10 OF 24 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-32086 DRUGU P Full-text
TITLE: Improved activity of **CPI-0004Na**, a new doxorubicin prodrug, in an experimental metastasis model.
AUTHOR: Dasnois L; Lebtahi K; Abarea Quinones J; Havaux N; Dubois V; Trouet A
CORPORATE SOURCE: Univ.Louvain-Cath.
LOCATION: Louvain La Neuve, Belg.
SOURCE: Int.J.Cancer (Suppl. 13, 435-36, 2002) 3 Ref.
CODEN: IJCNAW ISSN: 0020-7136
AVAIL. OF DOC.: Univerte Catholique de Louvain, Laboratory of Cell Biology, Louvain-La-Neuve, Belgium. (e-mail: dasnois@bani.ucl.ac.be).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
TI Improved activity of **CPI-0004Na**, a new doxorubicin prodrug, in an experimental metastasis model.
AB. . . developed to overcome the lack of selectivity and the side-effects responsible for the limited efficacy of the chemotherapeutic agents. Here, **CPI-0004Na**, a doxorubicin (DOX) prototype prodrug of this type, was evaluated in comparison with DOX against experimentally induced lung metastases in. . .
ABEX. . . the lungs' surface area occupied by metastases were determined. DOX had no effect on the number of lung metastases, while **CPI-0004Na** induced a 38,3% reduction. When considering the effect on the proportion of the lungs' surface covered by metastases, DOX induced. . .

L3 ANSWER 11 OF 24 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-42169 DRUGU C P S Full-text
TITLE: N-succinyl-(beta-alanyl-L-leucyl-L-alanyl-L-leucyl) doxorubicin: an extracellularly tumor-activated prodrug devoid of intravenous acute toxicity.
AUTHOR: Fernandez A M; Van derpoorten K; Dasnois L; Lebtahi K; Dubois V; Lobl T J; Gangwar S; Oliyai C; Lewis E R; Shochat D
CORPORATE SOURCE: Univ.Louvain-Cath.; Corixo
LOCATION: Louvain, Belg.; South San Francisco, Cal., USA
SOURCE: J.Med.Chem. (44, No. 22, 3750-53, 2001) 1 Fig. 2 Tab. 13 Ref.
CODEN: JMCMAR ISSN: 0022-2623
AVAIL. OF DOC.: Laboratory of Cell Biology, Universite Catholique de Louvain, Place Croix du Sud 5, B-1348 Louvain-la-Neuve, Belgium. (11 authors). (e-mail: fernandez@bani.ucl.ac.be).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB. . . pH, combined with its tendency to form large aggregates in aqueous solution. The negatively charged N-capped succinyl analog of (4), **CPI-0004Na** (5) was nontoxic given i.v., and was active i.p. vs. MCF-7/6 mamma tumor xenografts in mice.

L3 ANSWER 12 OF 24 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 7
ACCESSION NUMBER: 2001:435354 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100435354
TITLE: Optimization of peptide prodrug structure with a cancer cell peptidase enzyme screen.
AUTHOR(S): Nieder, Matthew [Reprint author]; Lobl, Tom; Nguyen, Thi;

Dubois, Vincent; Trouet, Andre; Horgan, Killian; Gangwar, Sanjeev
CORPORATE SOURCE: Coulter Pharmaceutical, Inc., South San Francisco, CA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 326. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA. March 24-28, 2001. American Association for Cancer Research.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Sep 2001
Last Updated on STN: 22 Feb 2002
IT . . .
Pharmacology; Tumor Biology
IT Parts, Structures, & Systems of Organisms
blood: blood and lymphatics; cancer cell
IT Chemicals & Biochemicals
CPI-0004Na: antineoplastic-drug, activation, peptide prodrug, pharmacokinetics; cellular endopeptidase; doxorubicin: antineoplastic-drug, sugar moiety

L3 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:202127 CAPLUS Full-text
TITLE: Sythesis OF **CPI-0004Na**, a doxorubicin tap prodrug
AUTHOR(S): Gangwar, Sanjeev; Lewis, Evan; Viski, Peter; Lobl, Tom; Trouet, Andre; Van Derpooten, Kim; Dubois, Vincent; Fernandez, A. M.
CORPORATE SOURCE: Dept. of Medicinal Chemistry, Coulter Pharmaceuticals, South San Francisco, CA, 94080, USA
SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001) MEDI-223
CODEN: 69FZD4
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
TI Sythesis OF **CPI-0004Na**, a doxorubicin tap prodrug
AB Many anti-tumor agents such as anthracyclines and vinca alkaloids have been developed in the last few years that are especially effective for the treatment of cancer cells. However, these mols. are often characterized in vivo by acute toxicity, especially marrow and chronic cardiac toxicity in the case of anthracyclines and a chronic neurol. toxicity in the case of the vinca alkaloids. **CPI-0004Na** is tumor activated peptide (TAP) prodrug of doxorubicin that is stable in blood and activated in the vicinity of tumors. **CPI-0004Na** is activated selectively in tumors in a MCF7 human tumor xenograft model thereby increasing its therapeutic index. As a result it can be given at a higher dose than doxorubicin and is effective in doxorubicin resistant tumors. The design and the synthesis of **CPI-0004Na**, a new TAP anticancer therapeutic, is presented.

L3 ANSWER 14 OF 24 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:658535 SCISEARCH Full-text
THE GENUINE ARTICLE: 434PJ
TITLE: Synthesis of **CPI-0004Na**, a doxorubicin

TAP prodrug.
AUTHOR: Gangwar S (Reprint); Lewis E; Viski P; Lobl T; Trouet A; Van Derpooten K; Dubois V; Fernandez A M
CORPORATE SOURCE: Coulter Pharmaceut, Dept Med Chem, S San Francisco, CA 94080 USA; Coulter Pharmaceut, Chem, S San Francisco, CA USA; Coulter Pharmaceut, Cell Biol, S San Francisco, CA USA
COUNTRY OF AUTHOR: USA
SOURCE: ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, (1 APR 2001) Vol. 221, Part 2, pp. U39-U39. MA 223-MEDI. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
ISSN: 0065-7727.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
TI Synthesis of **CPI-0004Na**, a doxorubicin TAP prodrug.

L3 ANSWER 15 OF 24 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:92575 TOXCENTER Full-text
COPYRIGHT: Copyright 2005 ACS
TITLE: Sythesis OF **CPI-0004Na**, a doxorubicin tap prodrug
AUTHOR(S): Gangwar, Sanjeev; Lewis, Evan; Viski, Peter; Lobl, Tom; Trouet, Andre; Van Derpooten, Kim; Dubois, Vincent; Fernandez, A. M.
CORPORATE SOURCE: Dept. of Medicinal Chemistry, Coulter Pharmaceuticals, South San Francisco, CA, 94080, USA.
SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001, (2001) pp. MEDI-223.
CODEN: 69FZD4.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2001:202127
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20040921
TI Sythesis OF **CPI-0004Na**, a doxorubicin tap prodrug
AB . . . chronic cardiac toxicity in the case of anthracyclines and a chronic neurol. toxicity in the case of the vinca alkaloids. **CPI-0004Na** is tumor activated peptide (TAP) prodrug of doxorubicin that is stable in blood and activated in the vicinity of tumors. **CPI-0004Na** is activated selectively in tumors in a MCF7 human tumor xenograft model thereby increasing its therapeutic index. As a result. . . given at a higher dose than doxorubicin and is effective in doxorubicin resistant tumors. The design and the synthesis of **CPI-0004Na**, a new TAP anticancer therapeutic, is presented.

L3 ANSWER 16 OF 24 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:297203 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100297203
TITLE: Synthesis of **CPI-0004Na**, a doxorubicin tap prodrug.
AUTHOR(S): Gangwar, Sanjeev [Reprint author]; Lewis, Evan; Viski, Peter; Lobi, Tom; Trouet, Andre; Van Derpooten, Kim; Dubois, Vincent; Fernandez, A. M.

CORPORATE SOURCE: Dept. of Medicinal Chemistry, Coulter Pharmaceuticals, 600 Gateway Blvd., South San Francisco, CA, 94080, USA Sanjeev_Gangwar@Coulterpharm.com
SOURCE: Abstracts of Papers American Chemical Society, (2001) Vol. 221, No. 1-2, pp. MEDI 223. print.
Meeting Info.: 221st National Meeting of the American Chemical Society. San Diego, California, USA. April 01-05, 2001. American Chemical Society.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Jun 2001
Last Updated on STN: 19 Feb 2002
TI Synthesis of **CPI-0004Na**, a doxorubicin tap prodrug.
IT Major Concepts
Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
CPI-0004Na: doxorubicin tumor activated peptide (TAP) prodrug

L3 ANSWER 17 OF 24 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:235859 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000235859
TITLE: Pharmacokinetics and tissue distribution of **CPI-0004Na**, a new prodrug of doxorubicin, in normal and tumor-bearing mice.
AUTHOR(S): Dubois, Vincent [Reprint author]; Fernandez, A. M.; Dasnois, L.; Collot, F.; Heylen, N.; Lobl, T.; Oliyai, C.; Shochat, D.; Trouet, A.
CORPORATE SOURCE: Coulter Pharm Inc, South San Francisco, CA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 523. print.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 01-05, 2000.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 2000
Last Updated on STN: 5 Jan 2002
TI Pharmacokinetics and tissue distribution of **CPI-0004Na**, a new prodrug of doxorubicin, in normal and tumor-bearing mice.
IT Major Concepts
Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
CPI-0004NA: antineoplastic-drug, doxorubicin prodrug, efficacy, pharmacokinetics, tissue distribution; doxorubicin: antineoplastic-drug

L3 ANSWER 18 OF 24 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-32080 DRUGU P Full-text
TITLE: Pharmacokinetics and tissue distribution of **CPI-0004NA**, a new prodrug of doxorubicin, in normal and tumor-bearing mice.
AUTHOR: Dubois V; Fernandez A M; Dasnois L; Collot F; Heylen N; Lobl T; Oliyai C; Shochat D; Trouet A
CORPORATE SOURCE: Coulter; Univ.Catholique-Louvain

LOCATION: South San Francisco, Cal., USA; Louvain, Belg.
SOURCE: Proc.Am.Assoc.Cancer Res. (41, 91 Meet., 523, 2000) ISSN: 0197-016X
AVAIL. OF DOC.: Coulter Pharma Inc., S. San Francisco, CA, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
TI Pharmacokinetics and tissue distribution of **CPI-0004NA** , a new prodrug of doxorubicin, in normal and tumor-bearing mice.
AB Pharmacokinetics and tissue distribution of **CPI-0004Na** , an extracellularly tumor-activated prodrug of doxorubicin (DOX), were evaluated in comparison with DOX, i.v. administered at equimolar doses in normal. . . that of DOX. Intact prodrug was the major species in plasma. Normal tissue exposure (AUC) to DOX after treatment with **CPI-0004Na** was much reduced cf. that after DOX (e.g. 90-95% reduction in the heart). Tumor AUC, however, was almost doubled. Results. . .

L3 ANSWER 19 OF 24 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:235857 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000235857
TITLE: **CPI-0004Na**: An extracellularly tumor-activated prodrug of doxorubicin.
AUTHOR(S): Trouet, Andre [Reprint author]; Passioukov, A.; Vanderpoorten, K.; Abarca-Quinones, J.; Lebtahi, K.; Baurain, R.; Dubois, V.; Lobl, T.; Gangwar, S.; Lewis, E.; Yarranton, G.
CORPORATE SOURCE: Coulter Pharm Inc, South San Francisco, CA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 522. print.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 01-05, 2000.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 2000
Last Updated on STN: 5 Jan 2002
TI **CPI-0004Na**: An extracellularly tumor-activated prodrug of doxorubicin.
IT Major Concepts
Pharmacology; Tumor Biology
IT Diseases
cancer: neoplastic disease
Neoplasms (MeSH)
IT Chemicals & Biochemicals
CPI-0004NA: antineoplastic-drug, tetrapeptidic derivative

L3 ANSWER 20 OF 24 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-32079 DRUGU P C S Full-text
TITLE: **CPI-0004NA**: an extracellularly tumor-activated prodrug of doxorubicin.
AUTHOR: Trouet A; Passioukov A; Vanderpoorten K; Abarca Quinones J; Lebtahi K; Baurain R; Dubois V; Lobl T; Gangwar S; Lewis E; Yarranton G
CORPORATE SOURCE: Coulter; Univ.Catholique-Louvain

LOCATION: South San Francisco, Cal., USA; Louvain, Belg.
SOURCE: Proc.Am.Assoc.Cancer Res. (41, 91 Meet., 522, 2000) ISSN: 0197-016X
AVAIL. OF DOC.: Coulter Pharma Inc., South San Francisco, CA, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
TI **CPI-0004NA**: an extracellularly tumor-activated prodrug of doxorubicin.
AB. . . well as for their reactivation by peptidases released by cancer cell lines. Based on these simple assays, a tetrapeptide derivative, **CPI-0004Na**, was selected. Lethality studies in the mouse showed that **CPI-0004Na** was 4-16x less toxic than DOX depending on the dosing route and the number of injections. Also, the chemotherapeutic superiority of **CPI-0004Na** as compared to DOX, was demonstrated in a number of human tumor xenograft models (mammary and colon carcinomas) using different. . .

L3 ANSWER 21 OF 24 ADISINSIGHT COPYRIGHT (C) 2005 Adis Data Information BV on STN

TX TEXT
Introduction:
Medarex and Diatos are developing a prodrug formulation of doxorubicin, called DTS 201(CPI 0004, **CPI 0004Na**, Super-Leu-Dox(TM)), using Tumour-Activated Peptide (TAP) platform technology. DTS-201 comprises a four-amino acid peptide chemically conjugated to the doxorubicin compound. When. . .

L3 ANSWER 22 OF 24 PHAR COPYRIGHT 2005 T&F Informa UK Ltd on STN
CN leucine-doxorubicin, Medarex
CN CPI-0004
CN **CPI-0004Na**
CN doxorubicin prodrug, Medarex
CN DTS-201
CN Super-Leu-Dox

L3 ANSWER 23 OF 24 PROUSDDR COPYRIGHT 2005 PROUS SCIENCE on STN
ACCESSION NUMBER: 2001:22 PROUSDDR Full-text

PROUS REFERENCES:
RefID: 613242 (Text Available)
Drug Data Report, Vol. 23, No. 6, pp 593, 2001

REFERENCE TEXT: RefID: 613242
ACTION - Tetrapeptide prodrug of doxorubicin shown to be inactive against tumor cells in vitro (IC50 > 50 mcM) but to be selectively activated by proteolytic cleavage in the vicinity of the tumor-resulting in specific tumor cytotoxicity in vivo. Compound was stable in human whole blood. It prolonged survival of mice bearing doxorubicin-resistant colorectal carcinoma LS174T or breast cancer MX-1 and doxorubicin-sensitive prostate cancer LNCaP. In these models it was significantly more effective and better tolerated than doxorubicin.

PATENT REFERENCES:

TITLE: Prodrug cpds. and process for preparation thereof
INVENTOR(S): Trouet, A.; Lobl, T.J.; Dubois, V.; Fernandez, A.-M.; Gangwar, S.; Lewis, E.; Nieder, M.H.; Viski, P.; Yarranton, G.T.
PATENT ASSIGNEE(S): Corixa
PATENT INFORMATION: JP 2003518000 20030603
WO 2000033888 20000615
PRIORITY INFORMATION: US 1998-111793 19981211
US 1999-119312 19990208

TITLE: CD10-activated prodrug cpds.
INVENTOR(S): Cardarelli, P.M.; Gangwar, S.; Nieder, M.H.; Bebbington, C.R.; Pickford, L.B.; Pan, C.
PATENT ASSIGNEE(S): Medarex
PATENT INFORMATION: EP 1404356 20040407
JP 2004537527 20041216
WO 2002100353 20021219
PRIORITY INFORMATION: US 2001-297596 20010611

REFERENCES:

(1) RefID: 572049, Periodic Publication
"CPI-0004Na: An extracellularly tumor-activated prodrug of doxorubicin"
Trouet, A.; et al., Proc Am Assoc Cancer Res, Vol. 41, (Abst 3328), 2000

(2) RefID: 572051, Periodic Publication
"Pharmacokinetics and tissue distribution of CPI-004Na, a new prodrug of doxorubicin, in normal and tumor-bearing mice"
Dubois, V.; et al., Proc Am Assoc Cancer Res, Vol. 41, (Abst 3329), 2000

(3) RefID: 612449, Periodic Publication
"Optimization of peptide prodrug structure with a cancer cell peptidase enzyme screen"
Nieder, M.; et al., Proc Am Assoc Cancer Res, Vol. 42, (Abst 1757), 2001

(4) RefID: 612450, Periodic Publication
"Evaluation of the pharmacokinetic properties of a doxorubicin prodrug in female ICR (CD-1) mice following intravenous bolus administration"
Tabrizi-Fard, M.; et al., Proc Am Assoc Cancer Res, Vol. 42, (Abst 1746), 2001

(5) RefID: 612451, Periodic Publication
"Cpi-0004, a doxorubicin prodrug that is inactive in vitro, prolongs survival of both doxorubicin-resistant and -sensitive human tumor-bearing"
Pan, C.; et al., Proc Am Assoc Cancer Res, Vol. 42, (Abst 1747), 2001

(6) RefID: 613026, Congress Literature
"Synthesis of CPI-0004Na, a doxorubicin tap prodrug"
Gangwar, S.; et al., ACS Natl Meet (221st Edition), April 1 2001-April 5 2001, San Diego, (Abst MEDI 223)

(7) RefID: 637021, Periodic Publication
"N-Succinyl-(beta-alanyl-L-leucyl-L-alanyl-L-leucyl)doxorubicin: An extracellularly tumor-activated prodrug devoid of intravenous acute toxicity"
Fernandez, A.-M.; et al., J Med Chem, Vol. 44, No. 22, pp 3750, 2001

(8) RefID: 675195, Periodic Publication
"CPI-0004Na, a new extracellularly tumor-activated prodrug of doxorubicin: In vivo toxicity, activity, and tissue distribution confirm tumor cell selectivity"
Dubois, V.; et al., Cancer Res, Vol. 62, No. 8, pp 2327, 2002

(9) RefID: 680141, Congress Literature
"Improved activity of CPI-0004Na, a new doxorubicin prodrug, in an experimental metastasis model"
Dasnois, L.; Dasnois, L.; Lebtahi, K.; Abarca-Quinones, J.; Havaux, N.; Dubois, V.; Trouet, A., UICC Int Cancer Congr (18th Edition), June 30 2002-July 5 2002, Oslo, (Abst P 958)

(10) RefID: 757746, Periodic Publication
"CD10 is a key enzyme involved in the activation of tumor-activated peptide prodrug CPI-0004Na and novel analogues: Implications for the design of novel peptide prodrugs for the therapy of CD10+ tumors"
Pan, C.; et al., Cancer Res, Vol. 63, No. 17, pp 5526, 2003

(11) RefID: 814512, Periodic Publication
"Anthracyclines: Molecular advances and pharmacologic developments in antitumor activity and cardiotoxicity"
Minotti, G.; et al., Pharmacol Rev, Vol. 56, No. 2, pp 185, 2004

CN DRUG NAME: CPI-0004
CPI-0004Na
CPI-004Na

L3 ANSWER 24 OF 24 SYNTHLINE COPYRIGHT 2005 PROUS SCIENCE on STN
ACCESSION NUMBER: 2002:4 SYNTHLINE
TITLE: N-Succinyl-(beta-alanyl-L-leucyl-L-alanyl-L-leucyl)doxorubicin: An extracellularly tumor-activated prodrug devoid of intravenous acute toxicity
AUTHOR(S): Fernandez, A.-M.; Van Derpoorten, K.; Dasnois, L.; Lebtahi, K.; Dubois, V.; Lobl, T.J.; Gangwar, S.; Oliyai, C.; Lewis, E.R.; Shochat, D.; Trouet, A.
SOURCE: J Med Chem (2001), 44(22), 3750

TITLE: Prodrug cpds. and process for preparation thereof
INVENTOR(S): Dubois, V.; Lewis, E.; Viski, P.; Gangwar, S.; Yarranton, G.T.; Nieder, M.H.; Fernandez, A.-M.; Trouet, A.; Lobl, T.J.
PATENT ASSIGNEE(S): Beckman Coulter, Inc.
PATENT INFORMATION: WO 2000033888
CN TAP-doxorubicin; Super-Leu-Dox; CPI-0004; CPI-004Na; **CPI-0004Na**
CN N-(N-(3-Carboxypropionyl)-beta-alanyl-L-leucyl-L-alanyl-L-leucyl)daunorubicin sodium salt; (8S,10S)-10-(3-(N-(3-Carboxy-1-oxopropyl)-beta-alanyl-L-leucyl-L-alanyl-L-leucylamido)-2,3,6-trideoxy-alpha-L-lyxo-hexopyranosyloxy)-8-(hydroxyacetyl)-6,8,11-trihydroxy-1-methoxy-7,8,9,10-tetrahydronaphthacene-5,12-dione sodium salt
RN 274912-87-7 (free acid)

=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	121.83	123.81

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

CA SUBSCRIBER PRICE -0.73 -0.73

FILE 'REGISTRY' ENTERED AT 17:13:03 ON 23 JUN 2005
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STRUCTURE FILE UPDATES: 22 JUN 2005 HIGHEST RN 852803-45-3
DICTIONARY FILE UPDATES: 22 JUN 2005 HIGHEST RN 852803-45-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when
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```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005. A new display format, IDERL, is now      *
* available and contains the CA role and document type information.  *
*                                                                    *
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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> S 274912-87-7/RN

L4 1 274912-87-7/RN

=> D L4 SQIDE TOTAL

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN **274912-87-7** REGISTRY
CN 5,12-Naphthacenedione, 10-[[3-[[N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CPI 0004Na
CN sALAL-Dox
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 4
NTE modified (modifications unspecified)

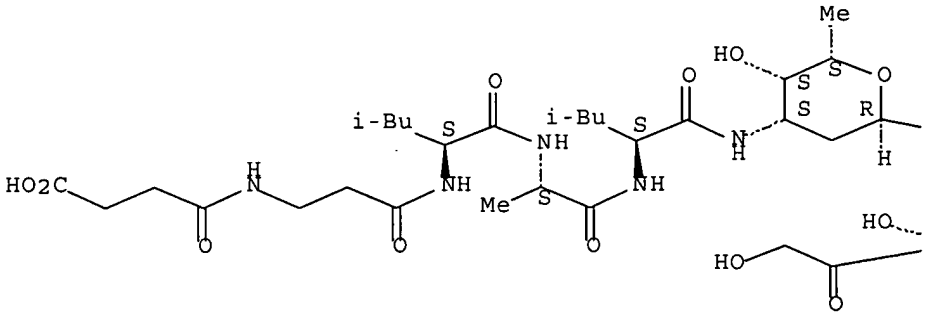
type	------ location ------		description
uncommon	Bal-1	-	-
modification	Bal-1	-	3-carboxy-1-oxopropyl<Suc>

SEQ 1 XLAL

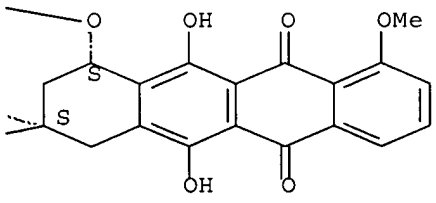
RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C49 H65 N5 O18
CI COM
SR CA
LC STN Files: CA, CAPLUS, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



10 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d l4 ed

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
ED Entered STN: 06 Jul 2000

=> d his ful

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(FILE 'HOME' ENTERED AT 17:07:21 ON 23 JUN 2005)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT,
CAPLUS, CEN, DDFB, DDFU, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL,
EMBASE, ESBIOBASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, JICST-EPLUS,
KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, ...' ENTERED AT 17:07:38
ON 23 JUN 2005
            SEA SALAL (W) DOX OR CPI (W) 0004NA
           ---------
           1    FILE ADISINSIGHT
           7    FILE BIOSIS
           2    FILE BIOTECHNO
           1    FILE CANCERLIT
           5    FILE CAPLUS
           7    FILE DDFU
           7    FILE DRUGU
           4    FILE EMBASE
           2    FILE ESBIOBASE
           1    FILE IFIPAT
           3    FILE MEDLINE
           2    FILE PASCAL
           4    FILE SCISEARCH
           8    FILE TOXCENTER
           2    FILE USPATFULL
           1    FILE PHAR
           1    FILE PROMT
           1    FILE PROUSDDR
           1    FILE SYNTHLINE
           1    FILE WPIDS
           1    FILE WPINDEX
L1          QUE PLU=ON  SALAL (W) DOX OR CPI (W) 0004NA
           ---------
            D RANK

FILE 'TOXCENTER, BIOSIS, DRUGU, CAPLUS, EMBASE, SCISEARCH, MEDLINE,
BIOTECHNO, ESBIOBASE, PASCAL, USPATFULL, ADISINSIGHT, CANCERLIT, IFIPAT,
PHAR, PROMT, PROUSDDR, SYNTHLINE, WPIDS' ENTERED AT 17:09:23 ON 23 JUN
2005
L2          54 SEA PLU=ON  L1
L3          24 DUP REM L2 (30 DUPLICATES REMOVED)
               D RANK
               D L3 1-24 IBIB KWIC

FILE 'REGISTRY' ENTERED AT 17:13:03 ON 23 JUN 2005
L4           1 SEA PLU=ON  274912-87-7/RN
               D L4 SQIDE TOTAL
               D L4 ED


FILE HOME

FILE STNINDEX

FILE TOXCENTER

FILE COVERS 1907 TO 21 Jun 2005 (20050621/ED)

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New CAS Information Use Policies, enter HELP USAGETERMS for details.

TOXCENTER has been enhanced with new files segments and search fields.
See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html for a description of changes.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 23 June 2005 (20050623/ED)

FILE RELOADED: 19 October 2003.

FILE DRUGU
FILE LAST UPDATED: 20 JUN 2005 <20050620/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

FILE CAPLUS

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FILE COVERS 1907 - 23 Jun 2005 VOL 142 ISS 26
FILE LAST UPDATED: 22 Jun 2005 (20050622/ED)

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FILE EMBASE
FILE COVERS 1974 TO 16 Jun 2005 (20050616/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

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FILE SCISEARCH
FILE COVERS 1974 TO 16 Jun 2005 (20050616/ED)

FILE MEDLINE

FILE LAST UPDATED: 22 JUN 2005 (20050622/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

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FILE BIOTECHNO
FILE LAST UPDATED: 7 JAN 2004 <20040107/UP>
FILE COVERS 1980 TO 2003.

>>> BIOTECHNO IS NO LONGER BEING UPDATED AS OF 2004 <<<

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN /CT AND BASIC INDEX <<<

FILE ESBIOBASE
FILE LAST UPDATED: 21 JUN 2005 <20050621/UP>
FILE COVERS 1994 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN /CC, /ORGN, AND /ST <<<

FILE PASCAL
FILE LAST UPDATED: 20 JUN 2005 <20050620/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN THE BASIC INDEX (/BI) FIELD <<<

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 23 Jun 2005 (20050623/PD)
FILE LAST UPDATED: 23 Jun 2005 (20050623/ED)
HIGHEST GRANTED PATENT NUMBER: US6910221
HIGHEST APPLICATION PUBLICATION NUMBER: US2005138714
CA INDEXING IS CURRENT THROUGH 23 Jun 2005 (20050623/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 23 Jun 2005 (20050623/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<

>>> records and may be searched in standard search fields, e.g., /PN, <<<
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>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

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FILE ADISINSIGHT

FILE COVERS 1986 TO 16 Jun 2005 (20050616/ED)
FILE LAST UPDATED: 16 JUN 2005 (20050616/ED)

FILE CANCERLIT
FILE COVERS 1963 TO 15 Nov 2002 (20021115/ED)

On July 28, 2002, CANCERLIT was reloaded. See HELP RLOAD for details.

CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE IFIPAT
FILE COVERS 1950 TO PATENT PUBLICATION DATE: 21 Jun 2005 (20050621/PD)
FILE LAST UPDATED: 22 Jun 2005 (20050622/ED)
HIGHEST GRANTED PATENT NUMBER: US6910221
HIGHEST APPLICATION PUBLICATION NUMBER: US2005132458
UNITERM INDEXING IS AVAILABLE IN THE IFIUDB FILE
UNITERM INDEXING LAST UPDATED: 13 Jun 2005 (20050613/UP)
INDEXING CURRENT THROUGH PAT PUB DATE: 4 Jan 2005 (20050104/PD)

INCL, INCLM, INCLS fields added. Please refer to ONLINE News for details.

FILE PHAR
FILE RELOADED May 4, 2003
FILE LAST UPDATED: Jun 20, 2005 (20050620/ED)

A new therapeutic code has been added to PHAR. See HELP THRCODES for details.

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FILE PROMT
FILE COVERS 1978 TO 23 JUN 2005 (20050623/ED)

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FILE PROUSDDR

FILE COVERS 1980 TO 2 May 2005 (20050502/ED)

FILE SYNTHLINE

FILE COVERS 1984 TO 15 May 2005 (20050515/ED)

FILE WPIDS
FILE LAST UPDATED: 21 JUN 2005 <20050621/UP>
MOST RECENT DERWENT UPDATE: 200539 <200539/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://thomsonderwent.com/coverage/latestupdates/ <<<

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http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501. PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-rev
FOR DETAILS. <<<

FILE REGISTRY
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STRUCTURE FILE UPDATES: 22 JUN 2005 HIGHEST RN 852803-45-3
DICTIONARY FILE UPDATES: 22 JUN 2005 HIGHEST RN 852803-45-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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     * The CA roles and document type information have been removed from *
     * the IDE default display format and the ED field has been added,    *
     * effective March 20, 2005.  A new display format, IDERL, is now     *
     * available and contains the CA role and document type information.  *
     *                                                                    *
     **********************************************************************

     Crossover limits have been increased.  See HELP CROSSOVER for details.

     Experimental and calculated property data are now available. For more
     information enter HELP PROP at an arrow prompt in the file or refer
     to the file summary sheet on the web at:
     http://www.cas.org/ONLINE/DBSS/registryss.html

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     8.85     132.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -0.73

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